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**INTERVENING NUTRITION AMONG COMMUNITY-DWELLING INDIVIDUALS WITH
ALZHEIMER'S DISEASE AND THEIR SPOUSES**

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ACADEMIC DISSERTATION

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LIST OF ORIGINAL PUBLICATIONS

I. Puranen T.M., Jyvakorpi S.K., Pitkala K.H., Eloniemi-Sulkava U., Poysti M.M. & Suominen M.H. 2013, "Nutritional intervention of patients with Alzheimer's disease living at home with their spouse: A randomized controlled trial. Baseline findings and feasibility", *Journal of Aging Research & Clinical Practice* vol. 2: no. 2, pp. 236-241.

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III. Suominen, M.H., Puranen, T.M., Jyvakorpi, S.K., Eloniemi-Sulkava, U., Kautiainen, H., Siljamaki-Ojansuu, U. & Pitkala, K.H. 2015, "Nutritional Guidance Improves Nutrient Intake and Quality of Life, and May Prevent Falls in Aged Persons with Alzheimer Disease Living with a Spouse (NuAD Trial)", *The journal of nutrition, health & aging*, vol. 19, no. 9, pp. 901-907.

IV. Puranen, T.M., Pitkala, K.H. & Suominen, M.H. 2015, "Tailored nutritional guidance for home-dwelling AD families: the Feasibility of and Elements Promoting Positive Changes in Diet (NuAD-Trial)", *The journal of nutrition, health & aging*, vol. 19, no. 4, pp. 454-459.

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LIST OF ABBREVIATIONS

AC Arm circumference	MCI Mild Cognitive Impairment
AD Alzheimer's Disease	MMSE Mini-Mental State Examination
ADAS-Cog Alzheimer's Disease Assessment Scale	MNA Mini Nutritional Assessment
ADL Activities of daily living	MNA-SF Mini Nutritional Assessment Short Form
AMC Arm muscle circumference	MST Malnutrition Screening Tool
ANCOVA Analysis of covariance	MUST Malnutrition Universal Screening Tool
APOE ε4 apolipoprotein E genotype	NCP Nutritional Care Plan
BMI Body Mass Index	NINCDS-ADRDA Alzheimer's Disease and Related Disorder's Association
CDR Clinical Dementia Rating Scale	NNR Nordic Nutrition Recommendations
CDT Clock-Drawing Test	NPI Neuropsychiatric Inventory
CG Control Group	NRS Nutritional Risk Screening-2002
CI Confidence Interval	NTB Neuropsychological Test Battery
COPD Chronic obstructive pulmonary disease	ONS Oral nutritional supplement
DHA Docosahexaenoic acid	RCT Randomized Controlled Trial
EE Energy Expenditure	REE Resting Energy Expenditure
EFSA European Food Safety Authority	SD Standard Deviation
EPA Eicosapentaenoic acid	SENECA Survey in Europe on Nutrition and the Elderly: concerned Action
FFQ Food frequency questionnaire	SNAQ Short Nutritional Assessment Questionnaire
FFM Fat free mass	TEE Total Energy Expenditure
FINGER The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability	TLC Total Lymphocyte Count
GNRI Geriatric Nutritional Risk Index	TP Total Protein
HRQoL Health Related Quality of Life	TSF Triceps Skinfold
IG Intervention Group	VaD Vascular Dementia
IADL Instrumental Activities of Daily Living	15D Health-related quality of life
MAC Mid-upper-arm circumference	

ABSTRACT

Nutritional status declines because of aging, functional disabilities and susceptibility to an increasing number of diseases. A poor nutritional status and inadequate nutrient intake increase morbidity, and inadequate protein intake in particular accelerates sarcopenia and functional decline. Nutritional problems such as a poor appetite and unintentional weight loss are common among individuals with Alzheimer's disease (AD), and their older spousal caregivers with comorbidities may also be at risk of malnutrition. The nutrient intake of community-dwelling individuals with AD may already be inadequate at the early stage of the disease. Some nutritional interventions have yielded positive outcomes, however. Oral nutritional supplements (ONSs) have managed to maintain and increase weight in AD sufferers, especially among institutionalized patients. Nutritional interventions among this group of people have not thus far estimated nutrient intake in detail, and no randomized, controlled studies have focused on tailored interventions among community-dwelling individuals with AD.

Objectives

The objective was to study the nutritional status and nutrient intake, of people with AD and their spouses, and to compare nutrient intake to national recommended levels. A further aim was to investigate the association between the caregiver's gender and the couples' nutrition. A randomized, controlled trial was conducted to examine the effectiveness of nutritional guidance on the AD victim's weight, nutritional status, energy and nutrient intake, quality of life and falls, and the intervention was assessed by means of qualitative analysis.

Subjects and Methods

The centralized drug reimbursement register (Kela) was used to recruit couples comprising an AD sufferer living at home with an older spousal caregiver. A total of 99 couples with completed food diaries were randomized into this trial. The intervention group (IG) received tailored nutritional guidance between four and eight times at their homes over one year, together with written nutritional material. The control group (CG) received booklet on healthy nutrition for older people. The primary outcome measure was the AD sufferer's weight change. The secondary outcome measures included nutritional status measured on the Mini-Nutritional assessment (MNA) test, nutrient intake calculated from three-day food diaries, health-related quality of life (HRQoL) measured on the 15D instrument, and falls measured from fall diaries provided by the spouses. Demographic data, and data on medications, cognition (Mini-Mental State examination, the MMSE and the Clinical Dementia Rating Scale, CDR), and functional status (Instrumental Activities of Daily Living, IADL) were also collected.

Results

The mean age of the individuals with AD was 77.4 years (SD 5.6), and of the spouses it was 75.2 years (SD 7.0). Of the former 69 percent were men. At baseline, 44 percent of the AD sufferers, and 16 percent of the spouses were at risk of malnutrition, whereas 56 and 84 percent, respectively, had a good nutritional status. The mean MMSE for those with AD was 19.3 (SD 5.6). There was wide variation in the intake of energy and nutrients. At baseline, the mean energy intake among those with AD was 1,897 kcal (SD 416) among the men and 1,313 kcal (SD 340) among the women, and the respective figures for spousal caregivers were 1,605 kcal (SD 458) and 1,536 kcal (SD 402). The mean protein intake of those with AD was 80 g for the men and 58 g for the women, and 70 g and 68 g, respectively, for the spouses. Among those with AD, 47 percent of the men and 71 percent of the women had a protein intake below one gram /bodyweight/kg, the respective figures for the spouses being 71 and 49 percent. In addition, almost half of the participants had a vitamin C intake of less than the recommended daily dose of 75 mg. The male gender of the caregiver was associated with poor energy and nutrient intake in the couple.

Tailored nutritional guidance had no effect on the weight of those with AD, but improved their nutrient intake and health-related quality of life. The differences between the IG and the CG were statistically significant with regard to protein and calcium intake. The mean change in protein intake was 0.05 g per bodyweight in kg (95% CI -0.06 to 0.15) in the IG, and -0.06 g per bodyweight in the CG (95% CI -0.12 to 0.02), $p = 0.031$. The respective changes in mean calcium intake were 85 mg (95% CI -24 to 194) and -17 mg (95% CI -98 to 65), $p = 0.025$. HRQoL improved by 0.006 (95% CI -0.016 to 0.028) in the IG, and declined by -0.036 (95% CI -0.059 to 0.013) in the CG, $p = 0.007$. The statistical analyses of nutrient intake and HRQoL were adjusted for age, gender, MMSE and BMI. In addition, those in the IG with AD had a significantly lower number of falls than those in the CG during the one-year intervention: 0.55 (95% CI 0.34 to 0.83) and 1.39 (95% CI 1.04 to 1.82) falls per person, $p < 0.001$, respectively.

Conclusions

The community-dwelling AD sufferers and their spousal caregivers were very heterogeneous in terms of nutrition, and a large proportion of the participants received inadequate amounts of several nutrients. Male caregivers may need tailored guidance on food-related activities. Tailored nutritional guidance improves both nutrition and the quality of life among those with AD, and may also prevent falls, and should therefore be part of their everyday care.

TIIVISTELMÄ

Ravitsemustila heikkenee iän, toiminnanvajausten ja sairauksien lisääntyessä. Huono ravitsemustila ja vähäinen ravintoaineiden saanti lisäävät sairastavuutta, ja erityisesti riittämätön proteiinin saanti kiihdyttää ikääntyneillä lihaskatoa, mikä johtaa toimintakyvyn heikkenemiseen. Ravitsemusongelmat, kuten ruokahalun heikkeneminen ja tahaton painonlasku ovat yleisiä muistisairailta ihmisillä, mutta myös iäkkäät puolisoahoitajat voivat olla ravitsemusriskissä. Kotona asuvien muistisairaiden ravinnonsaanti on tutkimuksissa ollut terveitä alhaisempaa jo sairauden alkuvaiheessa. Ravitsemusinterventioilla puolestaan on ollut myönteisiä vaikutuksia sekä muistisairaiden että heidän puolisoheidensa ravitsemukseen. Täydennysravintovalmisteilla on voitu ehkäistä muistisairaiden painon laskua erityisesti pitkäaikaishoidossa tehdyissä tutkimuksissa. Tutkimuksissa ei kuitenkaan ole arvioitu ravinnonsaantia tai ruokavalion laatua tarkemmin, eikä räätälöidyn ravitsemusohjauksen vaikuttavuutta ole tutkittu satunnaistetulla, kontrolloidulla asetelmalla.

Tutkimuksen tarkoitus

Tutkimuksessa selvitettiin millainen on kotona asuvien muistisairaiden ja heidän puolisoahoitajiensa ravitsemustila ja ravintoaineiden saanti verrattuna suosituksiin. Lisäksi tutkittiin, onko puolisoahoitajan sukupuoli yhteydessä tutkittavien ravintoaineiden saantiin. Räätälöidyn ravitsemusohjauksen vaikuttavuutta Alzheimer-potilaiden painoon, ravitsemustilaan, ravintoaineiden saantiin, elämänlaatuun ja kaatumisten ehkäisyyn tutkittiin satunnaistetulla, kontrolloidulla, tutkimusasetelmalla.

Aineisto ja menetelmät

Tutkittavat rekrytoitiin pääkaupunkiseudulta hyödyntäen Kansaneläkelaitoksen (Kela) lääkekorvaavuusrekisteriä. Tutkimuksessa päätulosmuuttujana oli tutkittavien painon muutos. Muita tulosmuuttujia olivat ravitsemustila, ravintoaineiden saanti, elämänlaatu, kaatumiset. Ravitsemustila arvioitiin Mini Nutritional Assessment (MNA) -testillä ja ravintoaineiden saanti laskettiin kolmen päivän ruokapäiväkirjoista. Terveysteen liittyvää elämänlaatua mitattiin 15D -kyselylomakkeella ja kaatumisia puolisoahoitajan kirjaaman kaatumispäiväkirjan avulla. Lisäksi tutkittavilta kerättiin sairaus- ja lääketiedot, ja kognitio (MMSE, CDR) ja toimintakyky (IADL) mitattiin. Ruokapäiväkirjojen tallentamisen jälkeen tutkittavat satunnaistettiin interventio ja kontrolliryhmiin. Interventioryhmään kuuluvat pariskunnat saivat räätälöityä ravitsemusohjausta kotonaan 4-8 kertaa vuoden aikana, heille annettiin kirjallista ravitsemusmateriaalia ja mahdollisuus osallistua 1-2 kertaa vuoden aikana ryhmätapaamiseen. Kontrolliryhmään kuuluvat saivat oppaan ikääntyneen ravitsemuksesta.

Tulokset

Tutkimukseen osallistui 99 pariskuntaa, jolta saatiin ruokapäiväkirjat. Muistisairaiden keski-ikä oli 77,4 (SD 5,6), ja puoliso hoitajien 75,2 (SD 7,0) vuotta. Muistisairaista 69 % oli miehiä. Alkutilanteessa muistisairaista 44 % ja puoliso hoitajista 16 % olivat MNA-testin perusteella aliravitsemusriskissä. Ravinnonsaanti vaihteli paljon. Alkutilanteessa energian saanti oli muistisairailla miehillä 1897 kcal (SD 416) ja naisilla vastaavasti 1313 kcal (SD 340). Puoliso hoitajista miehillä energian saanti oli 1605 kcal (SD 458) ja naisilla 1536 kcal (SD 402). Ravintoaineiden saanti oli suosituksia alhaisempaa usean ravintoaineen kohdalla. Muistisairaista miehistä 47 % ja naisista 71 % sai proteiinia alle 1 g kehon painokiloa kohden, vastaavat luvut puoliso hoitajamiehillä noin 71 %, ja naisilla 49 %. Noin puolet tutkittavista sai suosituksia vähemmän C- ja E-vitamiinia, ja folaatin saanti oli valtaosalla tutkittavista suosituksia alhaisempaa.

Räätälöidyllä ravitsemushoidolla ei ollut vaikutusta muistisairaiden henkilöiden painoon, mutta ohjaus paransi interventoryhmään kuuluvien ravintoaineiden saantia ja elämänlaatua. Proteiinin saanti parani interventoryhmässä 0,05 g kehon painokiloa kohden (95 % CI 0,06 - > 0,15), ja laski kontrolliryhmässä 0,06 g kehon painokiloa kohden (95 % CI -0,12 -> 0,02), (p = 0,03). Elämänlaatua mittaava 15D pistemäärä nousi interventoryhmässä (0,006 (95 % CI -0,016 -> 0,028), ja laski kontrolliryhmässä 0,036 (95 % CI -0,059 -> 0,013, p = 0,007). Lisäksi interventoryhmään kuuluvilla muistisairailla havaittiin merkitsevästi vähemmän kaatumisia ka 0,55/henkilö/vuosi (95 % CI 0,34 -> 0,83) verrattuna kontrolliryhmään, ka 1,39 kaatumista/henkilö (95 % CI 1,04 -> 1,82) vuoden intervention aikana. Analyysissä vakioitiin ikä, sukupuoli, BMI ja MMSE.

Johtopäätökset

Kotona asuvat muistisairaajat ja heidän puoliso hoitajansa ovat heterogeenisiä ravitsemuksen suhteen, ja suurella osalla tutkittavista usean ravintoaineen saanti jäi suosituksia alhaisemmaksi. Miehet puoliso hoitajina saattavat tarvita erityistä tukea ravitsemuksessa. Kotikäynneillä toteutettu räätälöity ravitsemusohjaus paransi tutkittavien muistisairaiden ravintoaineiden saantia, elämänlaatua, ja ehkäisi kaatumisia, joten se tulisi olla osa hyvää hoitoa.

1. INTRODUCTION

The population of older adults is increasing worldwide (World Population Ageing 2013). Finland is one of the fastest graying nations in Europe: the over-65s are estimated to comprise 26 percent of the Finnish population in 2030 (Official Statistics of Finland 2012), and the numbers in the oldest cohort, people over 75 years of age, are estimated to increase most rapidly (Statistics Finland's PX-Web databases 2015). The growing number of older adults will also lead to an increase in the number of people with dementia (Ferri et al. 2005). It is reported in a recent study that the prevalence of dementia in most Western countries has been stabilizing in recent decades, and that better living conditions and the prevention of vascular and chronic conditions may help to reduce the incidence (Wu et al. 2015).

Aging is accompanied with multiple chronic diseases, and nutrition has an important role in preventing and slowing their progression (Dwyer 2006). Loneliness, poverty and functional decline may increase the risk of malnutrition (Donini et al. 2013). Aging is associated with a diminishing appetite and decreased food intake (Hickson 2006, Malafarina et al. 2013a). Poor nutrition also impairs immunity (Lesourd 2006). Insufficient protein intake, together with immobility, accelerates sarcopenia, which leads to disabilities and falls (Morley et al. 2010, Bauer et al. 2013). Unintentional weight loss and malnutrition are associated with increased morbidity and mortality (Newman et al. 2001). Poor nutrition may also lead to deterioration in the quality of life and wellbeing (Keller et al. 2004b).

In Finland, approximately 130,000 people suffer from dementia, of which Alzheimer's disease (AD) is the most common accounting for 80 percent of cases (Current Care Guidelines 2010). AD leads to cognitive decline, disabilities and neuropsychiatric symptoms (Current Care Guidelines 2010). It is the most common reason for needing institutional care, and sufferers make extensive use of social and healthcare services (Sosiaali- ja terveystieteiden ministeriö 2012). The societal costs of AD are high, and are associated with the severity of the disease (Colucci et al. 2014).

Individuals with AD are prone to nutritional problems and weight loss, and malnutrition is common among them (Gillette-Guyonnet et al. 2007). The intake of several nutrients may be inadequate even during the early stage of the disease (Shatenstein et al. 2007). Several mechanisms may explain the weight loss: cognitive impairment leading to forgetfulness and skipping meals, olfactory dysfunction reducing appetite, psychological symptoms such as depression, and behavioral symptoms such as agitation and aggression (Gillette-Guyonnet et al. 2007). Furthermore, Alzheimer medications may have side effects such as nausea, impaired appetite and diarrhea (Current Care Guidelines 2010).

It has been suggested following some nutritional interventions that guidance from caregivers may improve the nutrition of community-dwelling AD patients (Riviere et al. 2001, Shatenstein et al. 2008), and could also slow down the cognitive decline (Riviere et al. 2001). However, these studies did not use rigorous methodology, and there were no randomized

trials. Oral nutritional supplements (ONS) have proven feasible in maintaining and gaining weight among AD patients in institutional settings (Manders et al. 2004, Hanson et al. 2011). However, none of these studies have shown improvements in hard outcomes such as disability, quality of life or the use of services.

Many AD patients in Finland live at their own homes, and are taken care of by spousal caregivers (Poysti et al. 2012). Taking care of someone with AD increases the caregiver's burden (Beerli et al. 2002). Many spousal caregivers are old, and they may have several comorbidities (Poysti et al. 2012). They may also have an increased risk of malnutrition (Rullier et al. 2014). No studies of the Finnish population thus far have focused on nutrition among community-dwelling individuals with AD and their spousal caregivers. The goal of the health policy is to support older adults to live in their own homes as long as possible (National Institute for Health and Welfare 2014). Nutrition is one of the factors affecting morbidity, disability, and the need for services among people with AD, and should therefore be investigated in this context.

This study explores nutrition among community-dwelling AD sufferers and their spousal caregivers, compares their nutrient intake to current recommendations, and investigates the effectiveness and feasibility of tailored nutritional guidance with regard to the participants' weight, nutrition, quality of life, and falls.

2. LITERATURE REVIEW

2.1 FACTORS RELATED TO NUTRITIONAL PROBLEMS IN OLD AGE

Aging is an evitable process, and may be characterized by chronic diseases and disabilities (Dwyer 2006). 'Older adults' in this work refer mainly to people aged 65 and above. Environmental factors have a strong influence on the aging process, and are assumed to make a 75-percent contribution to it, whereas genetic factors are estimated to have a 25-percent impact (Steves et al. 2012). Nutrition is one of the major factors that help to prevent or slow down the progression of many diseases (Dwyer 2006).

Malnutrition could be defined as a condition resulting from an imbalance between nutrient needs and intake (Harris & Haboubi 2005). It may result from either under- or over-nutrition, and both have negative effects on health (Guigoz 2006). Several types of risk factor have been identified: medical, social and psychosocial. These factors, together or combined, may be detrimental to the appetite, and cause difficulties in eating leading to poor nutrient intake and malnutrition (Hickson 2006). Furthermore, malnutrition may increase the risk of disease and infection, frailty and sarcopenia, and lead to a decreased quality of life (Keller et al. 2004b, Hickson 2006, Cruz-Jentoft et al. 2010, Cesari et al. 2014; see Figure 1).

2.1.1 Medical factors

Aging, *oral problems* and nutrition are closely linked. Loss of dentition, dry mouth, caries, periodontal diseases, gingivitis and mucosal lesions are common in old age, especially among the institutionalized (Saarela 2014), but community-dwelling older adults are also faced with this problem (Tada & Miura 2014). Masticatory problems may affect dietary habits, and are considered to be the major risk factor for poor nutrition among community-dwelling older adults (Tada & Miura 2014). Cross-sectional studies have shown that such problems are associated with lower vegetable and fruit intake (Marshall et al. 2002, Marcenes et al. 2003), and a low intake of several nutrients such as protein, fiber, thiamin, iron, folate, vitamin C, and carotenoids (Hung et al. 2003, Ervin & Dye 2009, Sahyoun et al. 2003), although some studies do not report an association (Shinkai et al. 2001, Bradbury et al. 2008).

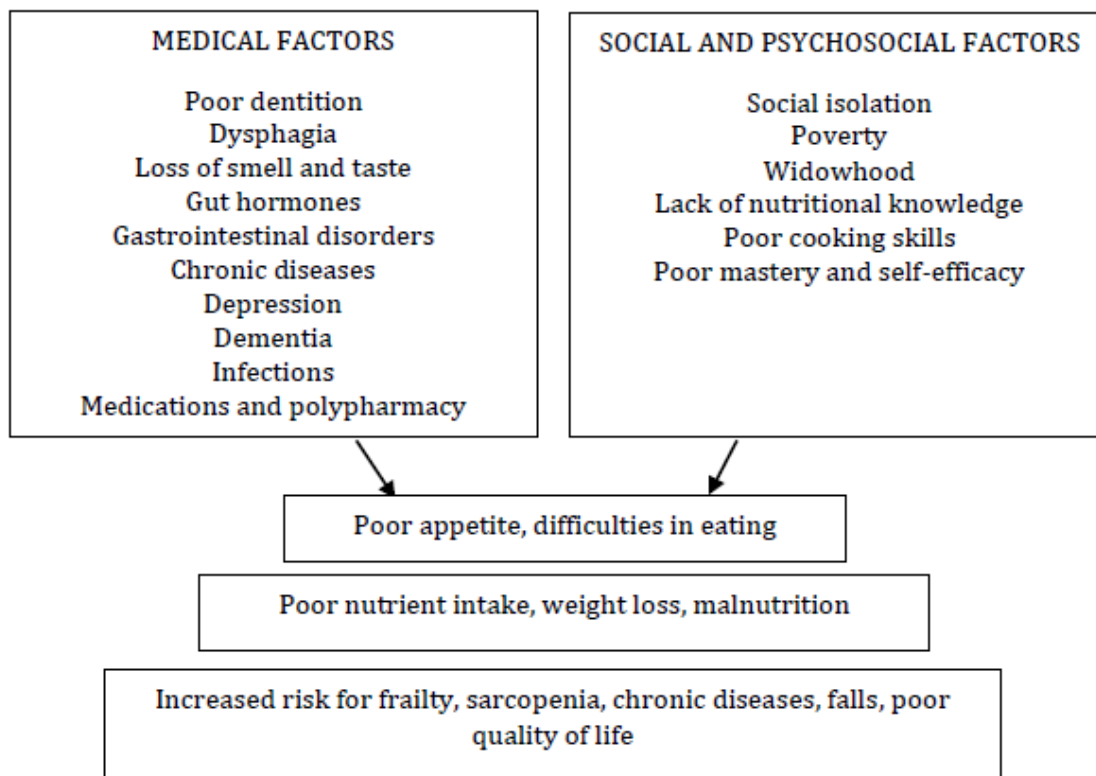


Figure 1. Possible factors contributing to weight loss and malnutrition in older adults (modified from Hickson 2006)

Swallowing difficulties are closely linked to nutritional problems. The risk increases with age, and such problems are more common among victims of stroke, dementia, and Parkinson's disease (Rofes et al. 2011). They are more prevalent among institutionalized (40-50%) than community-dwelling (7-22%) older adults (Easterling & Robbins 2008). Aging also affects the *olfactory system*, specifically the senses of taste and smell, which may diminish the appetite of older people (Hays & Roberts 2006, Hickson 2006). The aging process also has an effect on the *gastrointestinal (GI) tract*, decreasing esophagus sphincter tonus and motility (Ritz 2000). Gastric motility and stomach emptying slow down, and motility and intestinal transit time decrease (Ritz 2000). No significant changes occur in gastric acid secretion, however, except in the case of gastric atrophy (Ritz 2000). Approximately 10 percent of older people are estimated to suffer from vitamin B12 deficiency (Werder 2010), and the prevalence among those with dementia is 17 percent (Werder 2010). Impaired secretion of the intrinsic factor from the stomach is one of the possible causes of vitamin B12 deficiency (Werder 2010), which is also associated with multiple geriatric conditions such as cognitive decline, frailty, falls, functional decline, cachexia and anorexia of aging (Malouf & Areosa Sastre 2003).

Aging is accompanied with chronic diseases (Dwyer 2006). The associations between diseases and nutritional problems are multi-directional. Malnutrition may impair the immune function so the risk of contracting acute diseases may increase as a result of the decreased immunity, and chronic diseases may cause a loss of appetite (Lesourd 2006, Malafarina et al. 2013a). Diseases such as cancer and COPD may cause cachexia (Morley & Thomas 2008). Suffering from multiple diseases leads to the use of multiple medications, which may further affect the appetite and nutrition. *Polypharmacy* is common among older adults (Jyrkka et al. 2012), and high numbers of medications have been associated with a poor diet (Heuberger & Caudell 2011). Polypharmacy also increases the risk of drug-nutrient interactions, which may negatively affect the absorption of essential nutrients (Akamine et al. 2007). The side effects of various drugs may also affect nutrition by decreasing the appetite, causing gastrointestinal problems, and affecting nutrient intake (Uusvaara 2013). One of the side effects of drugs with anticholinergic properties, for example, is a dry mouth, which in turn may lead to oral problems (Uusvaara 2013). Many drugs used to treat AD may cause nausea, vomiting, and a poor appetite (Current Care Guidelines 2010). Psychological factors may cause a decrease in appetite, and lead to a poor nutrient intake (Hickson 2006), and according to a recent review, *depression* is the most common cause of anorexia in older people both in the community and in institutions (Morley 2013).

2.1.2 Social and psychosocial factors

Various social and psychosocial factors affect nutrition in older adults. *Social isolation* may have a negative effect among those with functional disabilities because it lowers the ability to do grocery shopping and to cook meals (Romero-Ortuno et al. 2011). *Poverty and a low income* may reduce the quality of the diet and increase the risk of malnutrition (Shahar et al. 2005, Dean et al. 2009, German et al. 2011, Holmes & Roberts 2011, Donini et al. 2013). An extensive cross-sectional study of 9,580 participants reported an independent association between a lower *education and social class* and lower fruit and vegetable intake, especially among men (Conklin et al. 2014). Furthermore, a *lack of nutritional knowledge* may be one reason for a poor dietary quality among older men (Baker & Wardle 2003, Hughes et al. 2004). *Living alone, loneliness, and widowhood* may affect eating through the simplification of food habits, and thus increase the risk of dietary inadequacy (Gustafsson & Sidevall 2002, Ramic et al. 2011, Shahar et al. 2001).

2.1.3 Weight

Weight loss among older adults may have serious consequences, especially if it involves a loss of muscle mass. It may be related to physiological or social factors, or a combination of both (Donini et al. 2003). Unintentional weight loss in particular may be indicative of a poor prognosis (Fried et al. 2001). *Anorexia of aging* is a serious weight-loss phenomenon that is characterized by a loss of appetite and reduced food intake (Malafarina et al. 2013a). According to a systematic review of 27 studies with a total of 6,208 participants, the prevalence of anorexia of aging is between 15 and 30 percent among the community-dwelling

population, 31 percent in nursing homes, and 31.5 percent among hospitalized patients (Malafarina et al. 2013a). It is more common in old age among women, people with disabilities and dependency in daily activities, and those with multiple diseases, cognitive decline and poor oral health (Malafarina et al. 2013a), and has been independently associated with mortality (Landi et al. 2012, Malafarina et al. 2013a).

Obesity is associated with multiple diseases in the adult population, but is not as simple to explain among older adults. The concept of the obesity paradox was introduced in the context of frail older people (McAuley et al. 2007), the paradox being that overweight and obese nursing-home residents seem to have the best prognosis (Veronese et al. 2015). However, it seems that weight changes during the life course are more reliable predictors than weight itself in old age (Strandberg et al. 2009). A healthy BMI for the adult population is under 25, but the results of epidemiological studies indicate that different BMI values might apply to older people. It was found in a combined analysis of 40 cohort studies that a low BMI (<20) was associated with an increased mortality risk, whereas a BMI of between 25 and 29.9 may present the lowest risk (Romero-Corral et al. 2006). However, severely obese patients, with a BMI of over 35, had an increased risk of cardiovascular mortality (Romero-Corral et al. 2006).

2.1.4 Frailty and sarcopenia

Weight loss and malnutrition in addition to immobility, chronic diseases and inflammation, may accelerate *frailty* and *sarcopenia* (Cruz-Jentoft et al. 2010, Bauer et al. 2013, Cesari et al. 2014). According to Fried's criteria, frailty is a clinical syndrome including at least three of the following features: weight loss (about 5 kg) in the past year, exhaustion, physical inactivity, a slow walking speed and a low grip strength (Fried et al. 2001). Symptoms, such as low mood, signs such as tremor and abnormal laboratory values, disease states and disabilities can be used to define frailty (Clegg et al. 2013). Some researchers suggest that the concept should include multiple dimensions such as cognitive, socioeconomic, and psychosocial frailty (Rockwood 2005, Kelaiditi et al. 2013). It affects protein metabolism by increasing muscle protein catabolism and further decreasing muscle mass (Chevalier et al. 2003), and has been associated with a higher age, being female, a lower income, a lower educational level, a higher number of chronic diseases, and lower muscle mass, density and functionality (Fried et al. 2001). Frailty predicts negative clinical outcomes such as disability, increased health costs, falls, hospital admission, the need for nursing-home care, and mortality (Shim et al. 2011, Gobbens et al. 2014).

The European Working Group on Sarcopenia in Older People (EWGSOP) defines *sarcopenia* as a syndrome characterized by a progressive and generalized loss of skeletal muscle and function, with a risk of adverse outcomes such as physical disability, a poor quality of life, and death (Cruz-Jentoft et al. 2010). The EWGSOP criteria for pre-sarcopenia include diminished muscle mass, for sarcopenia diminished muscle mass and muscle strength or performance, and for severe sarcopenia all three dimensions (Cruz-Jentoft et al. 2010: see Table 1).

Table 1. Stages of sarcopenia (Cruz-Jentoft et al. 2010)

	Muscle mass	Muscle strength		Performance
Pre-sarcopenia	↓			
Sarcopenia	↓	↓	OR	↓
Severe sarcopenia	↓	↓	AND	↓

The prevalence of sarcopenia varies according to the setting. Cruz-Jentoft et al. report in their systematic review that between one and 29 percent of community-dwelling older adults, 14-33 percent of patients in long-term care, and 10 percent of patients in acute hospital care suffer from sarcopenia (Cruz-Jentoft et al. 2014). Women are considered to be more vulnerable than men because they have less muscle mass to start with (Janssen et al. 2002, Beaudart et al. 2014). Sarcopenia may also be accompanied with obesity, and may be masked by an increased fat mass because the body weight remains stable (Morley 2001b). A loss of muscle mass is considered to be part of the normal aging process, however. Figure 2 shows the prevalence of sarcopenia in different age groups as reported in the Third National Health and Nutrition Examination Survey (NHANES III). (Janssen et al. 2002)

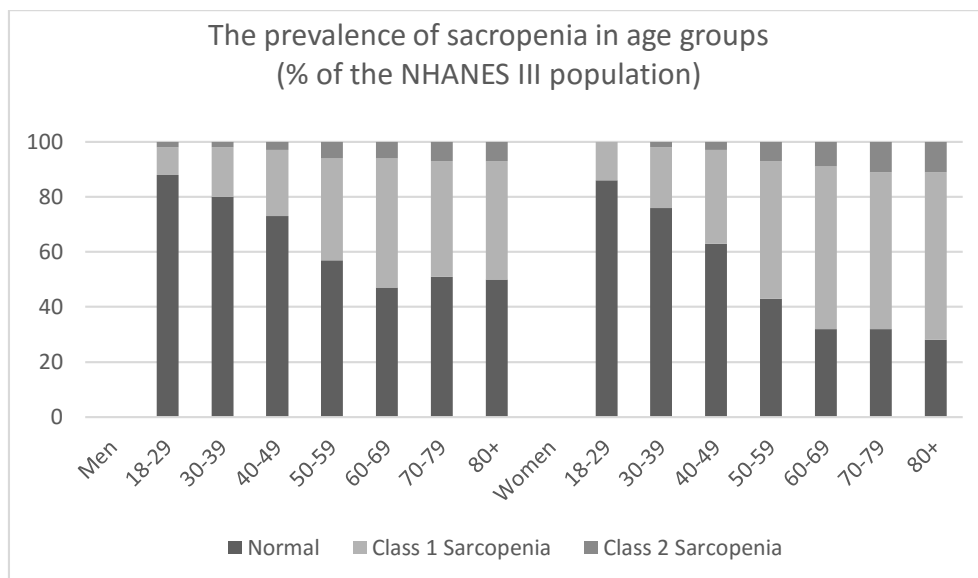


Figure 2. The prevalence of sarcopenia increases with age (modified from Janssen et al. 2002)

People with AD are prone to frailty and sarcopenia, as they tend to suffer from nutritional problems and weight loss (Gillette-Guyonnet et al. 2007), and a decreased lean body mass may furthermore be associated with brain atrophy and declined cognition among those with early-stage AD (Burns et al. 2010). Adequate energy and protein intake is essential in preventing sarcopenia, but a review concluded that nutritional supplementation is an effective treatment option, especially combined with physical exercise (Malafarina 2013b).

2.2 NUTRITION IN OLDER ADULTS

‘Nutrient’ refers to macronutrients including protein, carbohydrates and fat, as well as vitamins and micronutrients.

2.2.1 Energy and nutrient requirements

Energy requirement is the amount of energy needed to balance energy expenditure in order to maintain body mass, body composition and a level of physical activity, and to maintain good health (European Food Safety Authority, EFSA 2013). Total energy expenditure (TEE) decreases with age due to the decrease in resting energy expenditure (REE) and a decreased level of physical activity (PAL) (EFSA 2013). The decrease in REE results mainly from the reduction of fat free mass during aging (EFSA 2013). EFSA has published average energy-intake requirements for older adults engaging in different levels of activity (Table 2).

Finnish Nutritional Recommendations give energy reference levels that are similar to the EFSA levels, except that the former only include the 61-74 age group in the reference values for older adults (National Nutrition Council 2014), and no dietary reference values are given for the over-79s in the EFSA report because of the lack of studies (EFSA 2013). No specific recommendations for energy intake are published because the requirements differ widely according to sex, age, weight and activity (National Nutritional Council 2014).

Table 2. Average energy requirements for older adults engaging in different levels of physical activity (low, moderate, high) (EFSA 2013).

	REE kcal	AR at PAL = 1.4 (low) kcal	AR at PAL = 1.6 (moderate) kcal	AR at PAL 1.8 (high) kcal
MEN				
60-69 years	1440	2017	2305	2593
70-79 years	1416	1984	2267	2550
WOMEN				
60-69 years	1164	1628	1861	2093
70-79 years	1154	1614	1844	2075

REE = Resting energy expenditure, AR = Average requirement, PAL = Physical Activity Level

Finnish Nutritional Recommendations for older adults are based on Nordic Nutritional Recommendations (Suominen et al. 2014), and highlight five key messages: 1) Nutritional needs should be considered according to age and disability; 2) Weight, nutritional status, and food intake should be assessed regularly; 3) Food should contain an adequate amount of energy, protein, fiber, and fluids; 4) Vitamin D supplementation of 20 µg daily is recommended; and 5) Daily physical activity should be encouraged (Suominen et al. 2014). No mention is made of nutrient intake, which among the participants in this study is compared to the Finnish National recommendations (National Nutrition Council 2014) (Table 3).

Table 3. Nutrient recommendations (National Nutrition Council 2014)

	MEN		WOMEN	
Vitamins	61-74 years	≥75 years	61-74 years	≥75 years
Vitamin A, RE ¹	900	900	700	700
Vitamin D, µg	10	20	10	20
Vitamin E, α-TE ²	10	10	8	8
Vitamin B1, mg	1.3	1.2	1.0	1.0
Vitamin B2, mg	1.5	1.3	1.2	1.2
Niacin, NE ³	17	15	14	13
Vitamin B ₆ , mg	1.6	1.6	1.2	1.2
Folate, µg	300	300	300	300
Vitamin B ₁₂ , µg	2.0	2.0	2.0	2.0
Vitamin C, mg	75	75	75	75
Micronutrients	61-74 years	≥75 years	61-74 years	≥75 years
Calcium, mg	800	800	800	800
Phosphorus, mg	600	600	600	600
Potassium, g	3.5	3.5	3.1	3.1
Magnesium, mg	350	350	280	280
Iron, mg	9	9	9	9
Zinc, mg	9	9	7	7
Copper, mg	0.9	0.9	0.9	0.9
Iodine, µg	150	150	150	150
Selenium, µg	60	60	50	50

¹Retinol Equivalents ²Alpha-tocopherol equivalents ³Niacin equivalents

Protein recommendations for older adults

Finnish nutrition recommendations for older adults suggest a daily protein intake of at least 1.0 – 1.2 grams / bodyweight in kilograms (kg) to maintain muscle mass (Suominen et al. 2014), whereas the EFSA recommendation is the same as for the adult population as a whole (0.83 g/kg) (EFSA 2012).

Knowledge about protein requirements for older adults has increased in recent years, and it is suggested that they need more protein than younger adults to maintain good health and functionality, and to help recovery from illness (Bauer et al. 2013). Some age-related changes in protein metabolism occur, such as declining anabolic responses to ingested protein and high splanchnic extraction (Bauer et al. 2013). The suggested protein recommendations for healthy older adults are 1.0 - 1.2 g protein/ kg daily. The amount of dietary or supplemental protein for those with acute and chronic diseases depends on the disease and its severity, and the patient's nutritional status before and after the disease. The suggested daily intake for most of these older adults is 1.2 - 1.5 grams. Those with severe illnesses or who are malnourished may consume up to 2.0 g/ kg. Older adults with severe kidney disease need to limit their protein intake, however (Bauer et al. 2013). A low intake is associated with several adverse consequences. The extensive Women's Health Initiative Observational Study reported a strong, dose-responsive and independent association between higher protein consumption and a lower risk of frailty (Beasley et al. 2010). Adequate protein intake may also be essential

for bone health (Darling et al. 2009), and some studies indicate that increasing the intake improves bone-mineral density (Schurch et al. 1998, Tengstrand et al. 2007).

2.2.2 Methods of assessing nutrition

Nutritional status

The Mini Nutritional Assessment (MNA) test was developed to facilitate nutritional assessment among older adults >65 years, the aim being to give a rapid assessment of nutritional status in outpatient clinics, hospitals, and nursing homes (Vellas et al. 1999). The test includes several items: *Anthropometric measurements* including weight, height and weight loss, *global assessment* including six questions related to lifestyle, medication and mobility, a *dietary questionnaire* including eight questions about the number of meals, food and fluid intake, and autonomy, and a *subjective assessment* of health and nutrition (Vellas et al. 1999). The maximum MNA score is 30 points, which divides older adults into three groups: those with a good nutritional status (> 23.5 points), those who are at risk of malnutrition (17-23 points), and those who suffer from malnutrition (< 17 points) (Vellas et al. 1999).

The MNA is highly sensitive in screening those at risk of malnutrition (sensitivity 96%, specificity 98%: Vellas et al. 1999). It correlates with energy and nutrient intake, with anthropometric and biological nutritional parameters such as albumin, prealbumin, transferrin, cholesterol, retinol, alphetocopherol, 25-OH cholecalciferol and zinc, and with hematological measures such as hematocrit and hemoglobin, thus attesting to its sensitivity and specificity (Guigoz 2006). It is also associated with the Barthel Index measuring functional performance (Mirarefin et al. 2011). Further according to the MNA, malnutrition is associated with mortality (Persson et al. 2002, Guigoz 2006).

Rubenstein et al. (2001) created the short form of the MNA (MNA-SF) for screening purposes. It contains six items from the full MNA, and classifies older adults as well nourished or as at risk of malnutrition. The maximum score is 14, whereby ≥ 11 points indicates a normal nutritional status, and < 11 points indicates possible malnutrition and the need to carry out the full MNA (Rubenstein et al. 2001). Kaiser et al. (2009) further developed and validated the MNA-SF. The latest version contains six questions about changes in food intake, weight loss, mobility, psychological stress, neuropsychological problems, and BMI. If the BMI is not available, calf circumference may be used (Kaiser et al. 2009). A MNA-SF score of 12-14 points indicates normal nutritional status, a score of 8-11 points to a risk of malnutrition, and a score of 0-7 indicates malnutrition (Kaiser et al. 2009).

Other methods of measuring malnutrition focus mainly on hospital patients, and include the Malnutrition Universal Screening Tool (MUST) (Stratton et al. 2006), the Malnutrition Screening Tool (MST) (Marshall et al. 2015), the Short Nutritional Assessment Questionnaire (SNAQ) (Kruizenga et al. 2010), and Nutritional Risk Screening-2002 (NRS) (Neelemaat et al. 2011). The MUST estimates the effect of illness on nutrition intake, and has been used to

screen adult patients in hospital, community and other settings. It screens for weight loss in the previous six months (Kondrup et al. 2003). The MST is a short, two-question instrument focusing on recent unintentional weight loss and eating poorly (Marshall et al. 2015). The NRS includes the same questions as the MUST but the aim is to establish disease severity in order to estimate further nutritional needs, and it is designed for hospital use (Kondrup et al. 2003).

Nutrient intake

There are several methods for assessing nutrient intake, and a number of aspects should be considered in the case of older adults (van Staveren et al. 1994). First, the method to be used depends on the purpose of the study: whether nutritional data is needed on the individual or the group level (van Staveren et al. 1994). The target population also has to be considered, such as healthy versus care-dependent elderly people (de Vries et al. 2009). Food records or food diaries may be used to assess current nutrient intake. Retrospective methods assessing past dietary intake include food-frequency questionnaires (FFQ), and 24-hour or 48-hour recalls (Kroes et al. 2002). All retrospective methods are challenging among people with cognitive decline and the very old in that they require memory (de Vries et al. 2009). Observational methods or biomarkers should be considered in the case of older adults with disabilities such as memory disorders, and those living in institutions (de Vries et al. 2009).

Food diaries or food records can be used to assess nutrient intake in detail (Thompson & Bayers 1994). Food diaries tend to be collected over a period of between one and seven days (Kroes et al. 2002). All food and drinks consumed, and the amounts, are noted on the food-diary sheet (Thompson & Bayers 1994, Kroes et al. 2002). Precise weighing mechanisms may be used, or the portions described in terms of household measures (Kroes et al. 2002). These diaries provide good information about the current diet, and may be used to identify people with nutritional problems (Gariballa & Forster 2008). They are also useful in nutritional education, and in the setting of nutritional goals (Gariballa & Forster 2008). They may influence food intake, however, in that participants may consume more or less of certain foods, or eat different items than usual (Kroes et al. 2002). Both underreporting and over-reporting may occur, but under-reporting is assumed to be more common (Kroes et al. 2002), particularly among obese and weight-conscious people, especially women (Thompson & Bayers 1994). Certain foods and beverages such as fat and alcohol, respectively, are more commonly under-reported (Kroes et al. 2002). Keeping food records is time-consuming and the respondents have to be motivated (Thompson & Bayers 1994).

Twenty-four- and 48-hour recalls entail the gathering of information on food intake during the previous 24 or 48 hours by a trained interviewer with a good knowledge of nutrition and food (Thomson & Bayers 1994). Photographs of portion sizes may be used to assess the amounts of various items (Kroes et al. 2002). These recalls are quick and easy to do, and may also be administered on the phone. They require some short-term memory, and therefore may not be reliable among older adults (Kroes et al. 2002).

The Food Frequency Questionnaire (FFQ) is a dietary-assessment tool that could be used in large-scale epidemiological studies, and ranks participants as having low or high food intake. The aim is to assess consumption frequency with regard to certain food items, such as daily, weekly, monthly, or yearly. The comprehensive FFQ includes 50-150 questions on individual foods or food groups depending on the focus of the study, the aim being to measure several nutrients. Quantitative, semi-qualitative and qualitative FFQs are available. Quantitative measurements record only the usual number of times certain foods or drinks are consumed; semi-qualitative measures estimate standard portion sizes; and qualitative measurements cover any amounts of food consumed. The FFQ is easy to use, but it has to be validated within the population in which it is applied. (Kroes et al. 2002)

2.2.3 Nutritional status among older adults

According to a pooled analysis of published datasets including 24 studies and 4,507 participants from twelve countries, the prevalence of malnutrition in MNA terms varies depending on the setting: rehabilitation 50.5 percent, hospital 38.7 percent, nursing homes 13.8 percent, and the community 5.8 percent. The respective risks for malnourishment were 41.2, 47.3, 53.4, and 31.9 percent (Kaiser et al. 2010).

The results of a Finnish MNA study using combined data and including 4,949 participants from different settings showed that malnourishment was most common in long-term-care facilities (56.0%), and lowest among community-dwelling older adults (7.8%; Soini et al. 2011, see Figure 3).

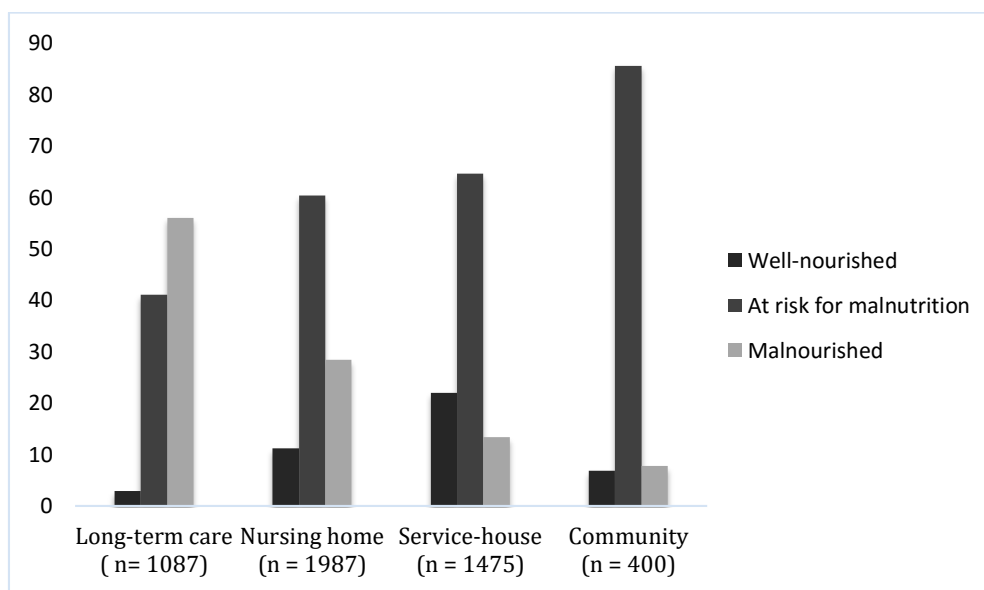


Figure 3. The prevalence of malnutrition (%) measured in accordance with the MNA in different settings in Finland (Soini et al. 2011)

However, a high percentage of the community-dwelling older adults in this combined data were at risk of malnutrition (85.5%), and the community-dwelling sample comprised older,

cardiovascular patients from The Drugs and Evidence-Based Medicine in the Elderly, DEBATE study (Strandberg et al. 2006a), indicating a high prevalence of malnutrition among this group of older adults (Figure 3).

MNA studies among community-dwelling older adults

Some recent cross-sectional studies report a prevalence of malnutrition of between 0-15 percent, and a risk of malnourishment of 12-39 percent among community-dwelling older adults (Bollwein et al. 2013, Donini et al. 2013, Turconi et al. 2013). It was found in a German cross-sectional study of 206 participants over 75 years of age that 15 percent of them were at risk of malnutrition according to the MNA, but none were malnourished (Bollwein et al. 2013). Furthermore, there was a close relationship between malnutrition and frailty according to Fried's criteria (Fried et al. 2001) in that 47 per cent of the frail, 12 percent of the pre-frail and two percent of the non-frail were at risk (Bollwein et al. 2013). It was found in an Italian study of 200 randomly selected, healthy older adults that 12 percent were at risk of malnutrition (Turconi et al. 2013): the majority of the participants had a low socio-economic status in terms of education and income, and only 30 percent of them were estimated to have an adequate diet according to the results of a questionnaire validated for the study. Another Italian study reported that more of the women were malnourished (15%) compared to the men (2%), the respective figures for malnourishment risk being 39 and 36 percent (Donini et al. 2013). It was further found in a Spanish study of over 20,000 community-dwelling older adults with a mean age of 75 years that four percent of them were malnourished, 25 percent were at risk, and >70 percent were well-nourished (Cuervo et al. 2009).

According to a Finnish cross-sectional study based on the MNA-SF, 15 percent of the 696 community-dwelling older adults in the sample were at risk of malnutrition (Nykanen et al. 2013), and a similar Norwegian cross-sectional study of over 2,000 participants reported similar rates of risk (14%; Soderhamn et al. 2012). Torres et al. (2014), using a proxy version of the MNA in their French study, found different rates of malnutrition among those living in the rural area (7%, compared to 19% among those in the urban sample). Factors that were independently associated with a poor nutritional status included being older, being female, a low BMI, a lower educational level and income, being widowed, having dementia, depressive symptoms, a loss of autonomy and an intake of more than three drugs (Torres et al. 2014).

2.2.4 Energy and nutrient intake among older adults

The majority of studies investigating nutrient intake among community-dwelling older adults are cross-sectional in design (de Groot et al. 1999, Foote et al. 2000, Marshall et al. 2001, 2002, Nydhal et al. 2003, Volkert et al. 2004, Roberts et al. 2005, Risonar et al. 2009, Helldan et al. 2013). Longitudinal data is available from the multinational Survey in Europe on Nutrition and the Elderly: a Concerned Action (SENECA study), which started in 1988 and recruited older adults born between 1913 and 1918 from nineteen European towns: the aim was to investigate the influence of dietary and lifestyle factors on health and survival (de

Groot et al. 1992). Several articles have been published based on SENECA data over the years, both cross-sectional (de Groot et al. 1999, Inelmen et al. 2000, Martins et al. 2002) and follow-up (Amorim et al. 1996, Moreiras et al. 1996, Toffanello et al. 2010, 2011).

According to the cross-sectional studies, the mean daily energy intake varied from about 1,100 kcal among women in the Philippines (Risonar et al. 2009) to about 2,200 kcal among men in Germany (Volkert et al. 2004). Lower energy intake has been reported in the over-80s than in 65-79-year-olds (Bates et al. 1999). Roberts et al. (2005), in turn, reported significant differences in energy intake between different BMI groups: the higher the BMI, the higher was the intake. They also found that older adults had surprisingly more varied diets than the younger group of 21-60-year-olds they included in their study. A Swedish study reported fairly low energy intake among women (Nydhal et al. 2003). (Table 4)

According to de Groot et al. (1999) the intake of 24 percent of men and 47 percent of women was at least one nutrient below the recommended level, and this persisted even among those who received ≥ 1500 kcal energy per day: 19 percent of men and 26 percent of women still had at least a one-nutrient deficit. Inadequate intake of iron and riboflavin was the most common. A German study based on both three-day food records and FFQs reported adequate intake of several nutrients among healthy community-dwelling older adults, but the median intake of fiber, calcium, vitamin D and folate proved to be inadequate (Volkert et al. 2004). A Finnish study based on 48-hour recall, with a study population of 65-74-year-olds, also showed recommended levels of nutrient intake, except for folate in both genders and vitamin D and iron among the women (Helldan et al. 2013). Inelmen et al. (2000), in turn, reported a high percentage of participants with a low calcium intake (men 77%, women 86%). A high proportion of the SENECA study population in Portugal showed low vitamin A (men 78%, women 73%) and calcium (men 39%, women 45%) intake levels (Martins et al. 2002).

Inadequate intake of folate, calcium, vitamin D, and vitamin E was reported in the American study (Marshall et al. 2002). According to the Swedish study, in turn, a large proportion of older women had low vitamin D, vitamin E, iron and folate intake compared to recommended levels, and the intake of protein, folate, and niacin, for example, was lower in the older than in the younger age group (Nydhal et al. 2003). The Irish study (Power et al. 2013) identified inadequate intake of several food nutrients (e.g. vitamin D, folate, zinc, vitamin C and calcium). Gender differences in food choices were revealed: women seemed to eat more fruit and vegetables, resulting in a better plasma α - and β -carotenoid status, and higher levels of vitamin C (Bates et al. 1999). Foote et al. (2000) also found that women were likely to eat more fruit and vegetables than men. Gariballa & Forster (2008) collected food diaries from a sample of older adults in hospital and after discharge, and found that energy and nutrient intake was lower at home: this may indicate post-discharge difficulties with shopping and cooking. Women were also reported to have a lower fiber intake than men, especially those in the oldest age group whose intake was about half of the recommended level (Bates et al. 1999), whereas in the Finnish study fiber intake was lower among men (Helldan et al. 2013).

Some *longitudinal studies* report a decrease in energy and nutrient intake with age (Amorim et al. 1996, Moreiras et al. 1996), whereas others show stable levels over four-to-10-year follow-ups (Jungjohann et al. 2005, Toffanello et al. 2010). According to a SENECA study, the mean energy intake of older adults decreased by about 1 mega joule or less (about 240 kcal), and protein intake decreased in almost all of the towns included in the research (Moreiras et al. 1996). Nevertheless, there was a high level of heterogeneity between the different towns across Europe and among the participants (Moreiras et al. 1996), and the use of nutrition supplements varied widely, from less than five to as much as 60 percent, for example (Amorim et al. 1996). Seventy-eight participants from the SENECA study in Italy were followed up ten years later: the mean energy intake was not significantly lower, but the percentage of those with an inadequate intake of several nutrients rose, and even those with a good nutritional and functional status were low in their intake of several nutrients, which may indicate poor dietary quality (Toffanello et al. 2010, 2011). (Table 4)

Nutrient intake among older adults is the most heterogeneous, and different study methods and study populations make it difficult to compare the results. Not only do the data-collection methods and recruitment practices differ, the nutrient databases may also vary in the countries concerned. Some studies showing a good nutrient intake among older adults and reporting their study population as being well-educated (Foote et al. 2000, Volkert et al. 2004) have also reported low levels of poor appetite, chewing or swallowing and other eating difficulties, and weight loss, indicating a healthy study population (Volkert et al. 2004).

Table 4. An overview of studies investigating energy and nutrient intake among community-dwelling older adults

Author/year	Participants	Methods	Findings (mean intakes/daily)	Context, comments
Cross-sectional studies				
Bates et al. 1999	N = 988 (48%women) Aged 65-79, 80+ years	4-day food diary	Energy 65-79 years: 8.07 MJ a (about 1,927 kcal)/men, 6.02 MJ (about 1,438 kcal)/women, in the 80+ age group: 7.42 MJ (about 1,772 kcal)/men, 5.67MJ (about 1,354 kcal)/women, protein 69g/men, 55g/women, and 65g/men, 50g, vitamin C 59 mg men/56 mg women, and 60mg, 46mg, respectively, inadequate intake of fiber, vitamin D, magnesium, potassium, and copper	The study was a National Diet and Nutrition Survey of people aged ≥ 65 years England
de Groot et al. 1999	N = 1005 (52% women) Mean age 77	Modified dietary history method	Inadequate intake > 1 nutrient: 24% /men and 47% /women, with energy intake above 1,500 kcal, 19% of men, and 26% of women, received inadequate intake of at least one nutrient	Nutritional data presented from nine centers, seven countries, SENECA, Europe
Foote et al. 2000	N = 1740 (29% women) Aged 51-80 years	FFQ	Energy intake 2,001 kcal (51-70 y) and 1,863 kcal (70-85 y)/men, and 1,571 kcal (51-70 y) and 1,555 kcal (70-85 y)/women, protein intake 76g (51-70 y)/men and 71g (70-85 y)/men, 63g (51-70 y)/women, and 60g (70-85 y)/women. >30% men and 60%women energy intake <1,600 kcal. >60% inadequate intake of vitamin D, vitamin E, calcium and folate	The study was part of the chemoprevention trial, participants highly educated, supplement use common USA
Inelmen et al. 2000	N = 190 Aged 70-75 years	Modified dietary history	Energy 2208 kcal/men, and 1742 kcal/ women, 77% of men, and 86% of women low calcium intake	SENECA, Italy
Marshall et al. 2001	N = 261, (67% women) Mean age 85 years	3-day food records	Energy (median, 25 th, 75 th) 1,617 kcal (1,364, 1924)/men; 1,467 kcal (1,212, 1,648)/women, protein intake (median, 25 th, 75 th) 57g (46, 67) Inadequate intake of folate, calcium, vitamin D, vitamin E	Energy intake presented in medians USA
Martins et al. 2002	N = 81 (49% women) Aged 81-86 years	24-h dietary recall	Low vitamin A intake 78% men, and 73% women Low calcium 39% men; 45% in women, low iron 49% men, 73% women	SENECA, Portugal
Nydhal et al. 2003	N = 135 (all women) Mean age 80 years	3-day food diary and 24-h recall	Energy 6.8 MJ (about 1,620 kcal) Vitamin D 4.8 mg, vitamin E 5.9 mg, iron 8.5 mg, folate 200 µg, selenium 29 mg	Sweden
Volkert et al. 2004	N =1,372 (58% women) Mean age 74/men, 77 years/women	3-day food records, FFQ	Energy (median) 2,207 kcal/men, 1,994 kcal/women, Protein 91g/men, and women 81g/women (1.2 g/kg body weight daily), median intake inadequate for fiber, water, calcium, vitamin D and folate	Educated and healthy population German
Roberts et al. 2005	N =1,174 (35% women) Mean age 71 (61 -90) years	24-h recall	Energy 2,034 kcal (all), energy BMI groups<22: 1,890kcal, 22-24.99: 1,935kcal, ≥25: 2,162 kcal, the differences were significant	Younger participants also included, only the results concerning older adults reported here USA

Gariballa & Forster 2008	N = 61 (42% women) Aged 66-86	7-day food diary	Energy 1,457 kcal, protein intake 64g, vitamin C 58mg, vitamin D 3 µg, folate 229 µg, calcium 703 mg	Validation study of food diaries, food diaries from hospital and at home (reported here)
Risonar et al. 2009	N = 88 (55%women) Mean age 69 (60-100) years	24-h recalls	Energy 1,180 kcal/men, 1090 kcal/women, protein intake 34 g/men, 29g/women, protein, fat, vitamins A and C, thiamin, riboflavin, iron and calcium) intake approximately 24-51% below recommended daily levels	The study population comprised rural Filipinos
Helldan et al. 2013	N = 413 (49%women) Mean age 69 (65-74) years	48-h recalls	Energy 1960 kcal/men and 1480 kcal/women, protein 16.9E% /men, and 17.2E%/women (about 83 g/men and 64 g/women), mean nutrient intakes adequate, except for folate intake, and vitamin D intake for women	Finnish population-based National Nutrition survey, conducted every five years Finland
Power et al. 2013	N = 208 (55% women) Mean age 75 years	FFQ	Median intake: Energy 2,008 kcal/men, 1,668 kcal/women, protein 79 g/men, 68g/women, vitamin C 96 mg/men, 115/women, folate 375 µg/ men, 358 µg women, vitamin E 30 mg/men, 28 mg/women, calcium 1056 mg/men, 1272 mg/women	Irish study, volunteers recruited from local healthcare and general practice centers, and via the media. Nutrient intake from both food and supplements
Longitudinal studies				
Amorim et al. 1996	N = 1,389 (53%women) Aged 70-75 years	Follow-up of four years, modified dietary history method	In several towns, the median intake of several nutrients (vitamins B1, B2, B6, C, and iron) decreased, over the follow-up period, the proportion of those with inadequate intake of several nutrients increased in most of the towns under study, the use of nutrition supplements varied greatly among the participants in different towns, from less than 5% to 60%	SENECA multi-center study, baseline data from 13, follow-up data from nine towns
Moreiras et al. 1996	N = 1,125 (51% women) Aged 70-75 years	Follow-up of four years, modified dietary history method.	At baseline, energy (all 13 cities): about 9.4 MJ (about 2,245 kcal)/men, and 7.8 MJ (about 1,860 kcal)/ women, protein about 80g/men, 67 g/women, the follow-up data (nine cities): Energy intake decreased by 1 MJ or less (about 240 kcal) during follow-up, protein intake decreased in all towns except one, large variation	SENECA multi-center study, baseline data from 13, follow-up data from nine towns
Jungjohann et al. 2005	N = 532 (70% women) Aged 60-91 years	Follow-up from 1994 to 2002, 3-day food record, FFQ	At baseline, energy in the younger age group 1,880 kcal/women, 2,300 kcal/men, older age group 1,826 kcal /women, 2,102 kcal, protein 17.6 E%/women, 16.2E%/men, 17.8E%, 17.1.E%, respectively, food, energy and macronutrient intake remained fairly stable over the study period	GISELA study, Germany, participants educated, physically active
Toffanello et al. 2010, 2011	N = 78 (56% women) Aged 70 - 75 years at baseline	Follow-up of ten years, modified validated dietary history	Energy declined from 2,178 to 1,997kcal/men; 1,795 to 1,644/women, not significant, after a decade, the prevalence of vitamin B2 and vitamin A deficiency rose to 50% of the sample, vitamin C deficiency increased to 4% in a decade in women	SENECA, Italy

E% = percentage of total energy intake, FFQ = food frequency questionnaire, kcal = kilocalorie, GISELA = A study of the nutritional and health status of an ageing population in Giessen, Germany, MJ = Mega joule, SENECA = Survey in Europe on Nutrition and the Elderly: a Concerned Action

2.2.5 Nutrition and the prevention of cognitive decline and dementia

The prevention of cognitive impairment in the elderly is assuming more significance given the aging population worldwide. It is estimated that delaying the onset of AD for five years could decrease the prevalence by as much as 50 percent in 50 years (Brookmeyer et al. 1998). The etiology of dementia and AD is multifactorial, reflecting both genetic and environmental factors. Physical activity and cognitive engagement have been associated with a decreased risk of AD, whereas smoking, depression, diabetes, and apolipoprotein E genotype (APOE ϵ 4) have been associated with an increased risk (Williams et al. 2010). The mechanisms behind AD have been under study for 30 years, and hallmarks of this disease such as extraneuronal senile plaques and intraneurofibrillary tangles are visible in the brain long before clinical symptoms such as cognitive impairment and dementia become apparent (Mi et al. 2013).

A growing body of epidemiological data confirms the role of a healthy diet and good nutrition in maintaining cognition (Otaegui-Arrazola et al. 2014), and a Mediterranean-type diet rich in fish, fruits, and vegetables, for example, and light or moderate alcohol consumption have been associated with a reduced the risk of cognitive decline (Panza et al. 2004, Feart et al. 2015). Malnutrition and deficiencies in nutrients such as omega-3 fatty acids, B-vitamins, and antioxidants are associated with cognitive impairment and an increased risk of cognitive decline and AD in several articles (Del Parigi et al. 2006, Steele et al. 2007, van der Beek & Kamphuis 2008, Solfrizzi et al. 2010, Mecocci et al. 2014, Ogawa 2014, Koyama et al. 2015). However, RCTs are needed to confirm these findings: some recent RCTs have already investigated the role of nutrition and other lifestyle factors in the prevention of cognitive decline (Martinez-Lapiscina et al. 2013, Ngandu et al. 2015, Valls-Pedred et al. 2015).

A Finnish multi-center study, The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), was conducted to investigate the effectiveness of multi-domain intervention in preventing cognitive decline in the general population with AD risk factors in a randomized controlled trial (Ngandu et al. 2015). A total of 1,260 individuals were randomized into a two-year intervention program that included nutritional guidance based on Finnish Nutritional Recommendations, and was conducted by a nutritionist in both individual and group sessions. The intervention, which also included physical exercise, cognitive training, social activities, and the monitoring and management of metabolic and vascular risk factors (Ngandu et al. 2015), positively affected the primary outcome, cognition, measured in accordance with the neuropsychological test battery (NTB) Z-score. The results after two years showed a 25-percent higher NTB Z-score in the IG compared to the CG. Significant intervention effects were also evident in secondary cognitive outcomes such as executive functioning and processing speed, but there was no significant effect on memory. According to the FINGER study, multi-domain intervention could help to maintain or improve cognition among older adults at risk of AD (Ngandu et al. 2015).

The aim of a Spanish RCT study, PREDIMED-NAVARRA, was to investigate the effect of a Mediterranean diet on cognition among 522 community-dwelling older adults with a mean

age of 75, and with high cardiovascular risk (Martinez-Lapiscina et al. 2013). The participants were randomized to the IG, which received nutritional education focused on a Mediterranean-type diet, or the CG that was given advice to follow a low-fat diet. The IG members also received either a liter of extra virgin olive or 30 g of mixed nuts weekly. The primary outcome measure was cognition assessment based on the Mini-Mental State Examination (MMSE) and the Clock-Drawing test (CDT), and the secondary outcomes included the incidences of dementia and mild cognitive impairment (MCI). Adherence to the diet was assessed by means of the FFQ during the 6.5-year follow-up. The Mediterranean diet with olive oil resulted in higher MMSE and CDT scores, with significant differences compared to the CG. Confounding factors such as APOE ϵ 4, cognitive impairment, smoking, physical activity, BMI, hypertension, dyslipidemia, diabetes, and alcohol and energy intake were adjusted for in the analyses (Martinez-Lapiscina et al. 2013.) The four-year intervention positively affected the primary outcome measure, NTB, in the groups on a Mediterranean diet supplemented with olive oil or nuts in the PREDIMED-NAVARRA sub-cohort (Valls-Pedret et al. 2015).

2.3 ALZHEIMER'S DISEASE AND NUTRITION

2.3.1 Alzheimer's disease

AD is a chronic and progressive neurodegenerative disease, and is the most common cause of dementia. Dementia could be defined as a loss of or decline in cognitive abilities, which leads to problems with the activities of daily living (ADL). Other common types of dementia include vascular dementia (VaD), mixed dementia, dementia with Lewy bodies, Parkinson's disease, frontotemporal dementia, Creutzfeldt-Jakob disease, and normal pressure hydrocephalus. MCI may be the earliest clinical manifestation of common age-related neurological disease. (Alzheimer's Disease International 2014)

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria, the progression of dementia is characterized by cognitive decline and the loss of functional skills in daily activities (American Psychiatric Association 1994). Dementia is also associated with neuropsychiatric symptoms and eating disorders (Cummings et al. 1997, Isaia et al. 2011). AD tends to require institutional care, and is therefore assumed to be one of the most expensive diseases for society (Alzheimer's Association 2014).

2.3.2 Weight loss in Alzheimer's disease

Weight loss in AD was first noted in 1906 by Alois Alzheimer in his case report of Ms. August D's progressive weight loss, which is one of the characteristics of the disease according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) (McKhann et al. 1984). Between 20 and 45 percent of community-dwelling older adults with AD are reported to suffer from weight loss (Droogsma et al. 2015b). A cross-sectional study based on combined data from 16,000 participants revealed an association between reported weight loss and AD severity (Albanese et al. 2013). According to a longitudinal study (Stewart et al. 2005), weight loss in old age may even precede dementia. Among AD sufferers it has predicted rapid cognitive decline, defined as a decrease of over three points in the MMSE score over six months, and mortality (White et al. 1998, Soto et al. 2012). Furthermore, caregiver burden has also predicted weight loss in AD sufferers (Gillette-Guyonnet et al. 2000). However, a recent retrospective, longitudinal study of 214 community-dwelling AD patients in the Netherlands reported no weight loss in a 3.5-year follow-up study (Droogsma et al. 2015a).

Factors related to weight loss in AD include brain atrophy, cognitive impairment, psychological and neurological problems, motor disturbances, poor oral health and swallowing difficulties, and changed food preferences (Gillette-Guyonnet et al. 2007, Alzheimer's Disease International 2014). These factors may also lead to a poor appetite, the inability to shop or prepare food, resulting inadequate energy and nutrient intake, and weight loss (Gillette-Guyonnet et al. 2007). (Table 5)

Table 5. Possible mechanisms of weight loss and under-nutrition among people with AD (Alzheimer's Disease International 2014)

Mechanism	Causes leading to weight loss and poor nutrition
Brain atrophy	Brain atrophy in regions governing the appetite may lead to a decrease in appetite and food intake, and further to weight loss and anorexia of aging
Cognitive impairment	Forgetting to eat meals Difficulties in using utensils and eating properly
Psychological symptoms	Depressive symptoms and apathy are associated with decreased food intake
Neuropsychiatric symptoms	Agitation, aggression, and attentional deficits may lead to aversive feeding behaviors
Motor disturbances	Wandering and declining practical skills may lead to interrupted meals and reduced eating
Oral health and swallowing difficulties	Tooth loss and mastication may affect food intake, olfactory dysfunction affects taste and may reduce the appetite, the risk of swallowing difficulties increases with disease severity
Food preferences	Changed food preferences or craving for foods that are rich in sugar

2.3.3 Nutritional status and nutrient intake among Alzheimer patients

The prevalence of MNA-assessed malnutrition among community-dwelling AD patients varies according to the setting. Rullier et al. (2013) found in their cross-sectional study that over half of their study population risked malnutrition, whereas Droogsma et al. (2013) reported that 14 percent were at risk among newly diagnosed AD patients in the Netherlands. In addition, whereas no cases of malnourishment were reported in the latter study, 23 percent of the subjects in the former, French study were assessed as malnourished. (Table 6)

A lower MNA score has been associated with age, the severity of cognitive impairment, behavioral disturbances, and decreased ADL functionality in several cross-sectional studies (Spaccavento et al. 2009, Isaia et al. 2011, Rogue et al. 2013, Rullier et al. 2013). Impairment in basic and complex daily functioning was independently associated with MNA in the above-mentioned Dutch study (Droogsma et al. 2013). In follow-up studies, a poor MNA-assessed nutritional status has predicted the more rapid aggravation of AD and NPI-assessed behavioral disturbances (Dumont et al. 2005, Guerin et al. 2005b, Vellas et al. 2005). The caregiver's burden was found to increase the risk of malnutrition in an Italian study during a short follow-up period of three months (Bilotta et al. 2010). However, only 33 percent of the caregivers were spouses, and about a half were sons or daughters. (Table 6)

Studies investigating nutrient intake among community-dwelling older adults with AD are scarce, partly because keeping food records requires memory. Shatenstein et al. (2007) managed to collect food diaries from their sample of AD subjects with the help of spousal

caregivers, and showed that the intake of energy and several nutrients such as dietary fiber, calcium, iron, zinc and vitamins K and A, and omega-3 fatty acids was significantly lower among those with AD compared to cognitively healthy controls assessed at the beginning and end of the one-year follow-up (Shatenstein et al. 2007). Another study among the same population reported that those with AD had significantly lower fruit and vegetable intake than the controls, and this resulted in a significantly lower vitamin K intake (Presse et al. 2008). Table 6 summarizes the MNA studies among community-dwelling individuals with AD, although people with other types of dementia are also included in some studies.

Table 6. An overview of studies investigating nutrition and associated factors among community-dwelling dementia patients

Author/year	Participants	Aim/Methods	Findings	Context, comments
Cross-sectional studies				
Presse et al. 2008	N = 31 (65% women) Mean age 78 years (+31 matched controls) Early stage AD, median MMSE 25 (13-30)	3-to-5-day food records provided by the spouses	Vitamin K intake was significantly lower in participants with AD compared to the controls, even following adjustment for energy intake, vitamin K indicates the fruit and vegetable intake, which was lower among those with AD	Participants recruited from three memory clinics, Canada
Spaccavento et al. 2009	N = 49 (65% women) Mean age 74 years Individuals with AD Mean MMSE score 17	To investigate the association between MNA cognition, functional status, and neuropsychiatric deficits	None were malnourished, 43% were at risk of malnutrition, those at risk tended to have more ADL- and IADL-assessed disabilities ($p = 0.03, 0.006$), and experienced more neuropsychiatric symptoms, such as apathy and motor disturbances	Participants recruited from memory clinics, Italy
Isaia et al. 2011	N = 130 (68% women) Mean age 78 (60-95) years AD, VaD, MCI Mean MMSE 17	To evaluate nutritional characteristics, MNA	The MNA score was associated with age ($p = 0.01$), cognitive impairment ($p = 0.001$), and behavioral disturbances ($p = 0.001$), the total score of the examined sample was inversely related to the total NPI score, and specifically with hallucinations ($p = 0.001$), depression ($p = 0.001$), nutritional disturbance ($p = 0.001$), wandering ($p = 0.001$) and hostile behavior ($p = 0.01$)	Of the participants, 18% had AD, 39% had MCI and 43% VaD, Italy
Saragat et al. 2012	N = 83 (68% women) Aged 66-96 (+91 age-matched controls)	To investigate the association between MNA and psycho-functional conditions (MMSE, GDS, ADL, IADL)	Malnourished 7% women; 0% men; at risk of malnutrition 51%/women and 27%/men, those with AD had a lower BIVA-measured body-cell mass compared to the controls, the lower MMSE and GDS decline among the former were associated with obesity	Participants recruited from the Alzheimer Center, Italy
Droogsma et al. 2013	N = 312 (62%women) Mean age 78 Newly diagnosed AD Mean MMSE 20.6	To study the prevalence of malnutrition and associated factors	None were malnourished, 14% were at risk of malnutrition, those with AD and at risk of malnutrition were more impaired in daily functioning than the well-nourished ($p = 0.001$)	Newly diagnosed AD patients from Memory clinics The Netherlands
Roque et al. 2013	N = 940 (68%women) Mean age 78 years/men, 81 years/women. Persons with different types of dementia	To evaluate nutritional status and associated factors	Malnourished 6%/men, and 4%/women, at risk of malnutrition 39%/men, 44%/women, malnutrition was associated with an advanced age, decreased cognition and functionality, and increased caregiver's burden	Demented participants with AD, VaD, mixed dementia, Lewy Bodies frontal lobe and others Spain
Rullier et al. 2013	N = 56 (43% women) Mean age 81 years, 71 years for caregivers. Mean MMSE 16.5	To study the nutritional status of individuals with AD and their caregivers, and associated factors	AD: Malnourished 23%, at risk of malnutrition 59% Caregivers, 5% and 32% respectively, the MNA of AD was strongly and inversely associated with the ADL score, and strongly associated with the MNA of the family caregiver	Community-dwelling dyads, with a caregiver with normal cognition France

Continues				
Author/year	Participants	Aim/Methods	Findings	Context, comments
Follow-up studies				
Dumont et al. 2005	N = 312 Mean age 75 years	To investigate factors affecting the progression of AD during a one-year follow-up	Rapid cognitive loss (≥ 4 points loss in MMSE) associated with a low MNA score	Participants from the ELSA study, France
Guerin et al. 2005b	N = 561 (69% women) Mean age 78 years	To describe the cognitive and behavioral characteristics of older adults with different nutritional statuses, with a one-year follow-up	At baseline 18% were at risk of malnutrition, 3% were malnourished, those who were well nourished or at risk of malnutrition differed from the malnourished in terms of age, IADL-measured functionality, and NPI-measured neuropsychiatric symptoms, after one year, (n =361), malnourished > higher NPI	The number of drop outs after one year (35%) was high, France
Vellas et al. 2005	N = 523 Mean age 75 years (MNA>23.5), 77 years (MNA <23.5)	To determine the impact of nutritional status on the evolution of AD during a one-year follow-up	At baseline, 26% were at risk of malnutrition, after one year, those with a malnutrition risk at baseline tended to show a rapid loss in MMSE (≥ 3 points/year) compared to those with a good nutritional status	Participants from the REAL.FR study, France
Shatenstein et al. 2007	N = 36 (+ 58 age-matched controls)(68% women) Mean age 78 years Early stage AD	Nutrient intake among those with AD compared to controls, 24-hour recalls four times during the follow-up year	The mean energy intake during the one-year follow-up: those with AD 1,527 -> 1,486 kcal, healthy controls 1,781 ->1,803 kcal, the respective figures for mean protein intake: 64 -> 63 g, and 74 -> 73 g	Recruited from memory clinics, people with AD living with a spouse, Canada
Ousset et al. 2008	N = 160 (68% women) Mean age 76 (53-89) years Mild AD France	To investigate the factors associated with weight loss in AD	At baseline, 28% at risk of malnutrition, a mean MNA score of 25.1 (16-30), After one year, 53% remained stable according to the CDR, and those who progressed had a poorer nutritional status at baseline	The REAL.FR study, France
Bilotta et al. 2010	N = 105 (68% women) Mean age 83 years Mild to moderate AD	To investigate the association the caregiver's burden and weight loss among AD patients during a 3-month follow-up	At baseline, 20% malnourished, 51% at risk of malnutrition, (MNA-SF), after three months: the caregiver's higher burden increased the risk of malnutrition	Of the caregivers 51% were sons and daughters, and 33% were spouses Italy

ADL = Activities of daily living (Katz et al. 1970), BIVA: Bioelectrical Impedance Vector Analysis, BMI = Body mass index, CDR =The Clinical Dementia Rating, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders ELSA study = French Longitudinal study investigating progression of AD, GDS = Geriatric Depression Scale (GDS), IADL = Instrumental Activities of Daily Living, MCI = Mild cognitive impairment, MMSE = Mini Mental State Examination, MNA = Mini Nutritional Assessment, NINCDS- ADRDA = National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association, NPI = Neuropsychiatric Inventory, REAL.FR = longitudinal multicenter cohort study in 16 University Hospitals in French, VaD = Vascular Dementia

Plasma nutrient levels among Alzheimer subjects

A systematic review and meta-analysis of 80 studies with over 16,000 participants revealed lower levels of plasma nutrient among the AD subjects than among the controls. The meta-analysis revealed significantly lower levels of folate and vitamin A, vitamin B12, vitamin C, and vitamin E in those with AD: lower levels of zinc and vitamin D were also found, but the differences were not significant. In general, low levels of plasma nutrient are assumed to follow protein and energy malnutrition, although in the meta-analysis the differences between the AD subjects and the controls also remained significant for folate, and vitamin B12, vitamin C and vitamin E, even among subjects with no reported energy or BMI-estimated protein malnutrition, MNA or serum albumin. (Lopes da Silva et al. 2014)

Lopes da Silva's (2013) review also includes studies reporting levels of omega-3 fatty acids, B-vitamins, and calcium, but these studies were not included in the meta-analysis, either because there were too few, or because they used different methods for measuring plasma levels (Lopes da Silva et al. 2013). Compared with people without AD, the docosahexaenoic acid (DHA) levels were lower in three studies, but not in one, and one study reported higher DHA plasma levels among the AD subjects compared to the controls. Four studies reported lower eicosapentaenoic acid (EPA) levels in the AD subjects than in the controls, and one study found no significant differences. Lower levels of plasma vitamin B1 were reported in one study, and lower B6 in another. One study reported lower plasma calcium levels in those with AD compared to the controls, although another two studies found no significant differences in levels. (Lopes da Silva et al. 2014)

A recent Dutch study compared drug-naïve AD subjects to healthy controls and found that those with mild AD had significantly lower plasma selenium and uridine levels (Olde Rikkert et al. 2014). Their MNA score was also lower, but this was not indicative of malnutrition (Olde Rikkert et al. 2014).

2.3.4 Nutritional interventions among Alzheimer patients

There are few studies on nutritional intervention among community-dwelling individuals with AD (Droogsma et al. 2014). Droogsma et al. (2014) conducted a systematic review of RCT studies among community-dwelling AD subjects at risk of malnutrition according to the MNA, MUST or NRS-2000 criteria, and found only one, Lauque et al. 2004, which included those at risk of malnutrition, at least. Interventions have included nutritional education (Riviere et al. 2001, Pivi et al. 2011, Salva et al. 2011), and ONSs (Lauque et al. 2004, Planas et al. 2004, Pivi et al. 2011). Table 7 summarizes the studies on nutritional interventions among community-dwelling individuals with AD. Four of them were randomized, controlled trials (Lauque et al. 2004, Planas et al. 2004, Pivi et al. 2011, Salva et al. 2011), and one was a non-randomized trial (Riviere et al. 2001). The nutritional intervention reported by Shatenstein et al. (2008) is presented separately with two case studies on page 40.

A French study investigated the extent to which nutritional education targeted at spousal caregivers could prevent weight loss among their AD charges (Riviere et al. 2001). The participants were recruited from day hospitals in France, Italy and Spain, and the mean age was 73.3 years in the IG and 75.4 years in the CG. The mean MMSE was about 15 points, and the mean MNA score was 23 and 24 in the IG and the CG, respectively. The nutritional education included nine one-hour sessions over one year, covering aspects such as the consequences of weight loss, coping with stress among caregivers, how to assess nutritional status in line with the MNA, nutritional and food recommendations, tips for increasing protein intake, eating disorders, and practical dietetics. Caregivers also received calendars to record the weight of their spouses, and brochures on diet and physical exercise. The caregivers were advised to call the dietician if their spouse lost more than 2 kg in weight. The intervention resulted in weight gain (0.7 ± 3.6 kg) in the IG, and weight loss (-0.7 ± 5.4 kg) in the CG. However, the difference between the groups was not significant following adjustment for baseline differences in the caregiver's age, nutritional status, eating disorders, and depression. The percentage of participants with significant weight loss decreased during the year, however. The MNA remained stable in the IG, but decreased in the CG, and the difference was significant. Cognition measured in accordance with the MMSE differed significantly between the groups, and the caregiver burden measured on the Zarit questionnaire showed no improvement. A limitation of the study was that it was not randomized. (Riviere et al. 2001)

A French randomized, controlled study investigated the effects of ONSs on body weight, body composition, nutritional status, and cognition in individuals with AD at risk of malnutrition according to the MNA, the mean BMI of participants recruited from geriatric wards and day-care centers being 22.4 kg/m^2 (Lauque et al. 2004). The IG received ONSs containing 300-500 kcal daily for three months in addition to their regular diet. At baseline, the mean age was 60.5 years in the IG and 64.8 years in the CG, and the mean MNA was 22.9 and 24.3 points, respectively. These variables differed between the groups and were adjusted for in the analyses. The mean MMSE of the participants was 15 points. The intervention resulted in increased weight and fat-free mass (FFM), but no changes were observed in dependence

measured in accordance with the ADL, cognitive function measured in accordance with the MMSE, or biological markers such as serum albumin and C-reactive protein. According to the authors the ONSs were practical and well received by the participants. There were nine drop-outs, and intention-to-treat analyses were carried out. (Lauque et al. 2004)

Planas et al. (2004) recruited 44 participants with a normal nutritional status into a randomized trial investigating the effect of ONSs with or without micronutrient enhancement on weight and disease progression. All the participants received energy-dense ONSs twice daily, containing total of 500 kcal (comprising 45% carbohydrates, 25% fat, and 30% protein). The ONSs with micronutrient enhancement included vitamin E, vitamin C, vitamin B12, folate, zinc, copper, manganese, whey protein, and arginine. The participants were recommended to eat three regular meals and to administer ONSs between them. Energy intake increased significantly in both groups after the six-month intervention, but no differences between the groups emerged. There was a visible trend towards an increased BMI, but again no significant difference between the groups. Significant increases in triceps skin fold thickness (TSF) and mid-upper-arm circumference (MAC) ($p < 0.001$ for both) were observed in both groups after the intervention. It had no effect on feeding behavior or cognition, but there was a significant decrease in serum cholesterol level in the micronutrient-enhancement group. The study had a randomized design, but the randomization is not described in the article. In addition, several outcomes are presented, but the primary outcome measure is not mentioned. (Planas et al. 2004)

Pivi et al. (2011) compared the effects of nutritional education and ONSs on nutritional status among subjects with AD in a randomized controlled trial lasting six months. The mean MMSE score at baseline was 12 points, and 40 percent of the participants were in the moderate stage of the disease according to the CDR. The participants were assigned to one of three groups: the education group, the supplementation group, or the CG. Members of the education group participated in the education program ten times. Each education session included a maximum of ten caregivers, the aim being to foster interaction between professionals and caregivers. The themes included the importance of nutrition in AD, behavioral changes related to eating and nutrition, preparing attractive meals, dealing with a poor appetite, and information on food supplementation and other health-related issues such as constipation, hydration and drugs. The supplementation group received ONSs twice daily, containing altogether 680 kcal and 25.6 g protein. The primary outcome was nutritional status assessed in accordance with anthropometric and biochemical data. The anthropometric measurements included height, weight, BMI, arm circumference (AC), arm muscle circumference (AMC), and TSF, whereas the biochemical measures included total protein (TP), serum albumin, and total lymphocyte count (TLC). Cognition was measured in accordance with the MMSE and the CDR. ONSs supplementation improved weight, BMI, and AMC compared to the other groups after the six-month intervention. There was no statistical difference in TSF between the groups, but the BMI increased in the education group compared to the CG. ONSs supplementation also had a positive effect on the TP and total lymphocyte levels, the difference being significant compared to the CG, and the education group also showed higher total lymphocyte levels compared to the controls. There were no statistically significant differences in serum albumin

among the three groups. The primary outcome measure is not stated clearly in the article, and no information about the randomization is given. (Pivi et al. 2011)

A Spanish randomized, multi-center cluster study investigated the effectiveness of a health and nutrition program (NutriAlz) on the AD subjects' autonomy, measured ADL and IADL scores, and MNA, and on the Zarit score measuring the caregiver's burden (Salva et al. 2011). The participants were recruited from 11 outpatients' clinics and day hospitals. A standardized protocol for feeding and nutrition was implemented in the intervention centers. The protocol included: 1) a personalized presentation and a briefcase of booklets about nutrition, booklets about physical exercise, and information about available services, which was given to the patients and their caregivers; 2) training sessions for families and caregivers offered four times covering different themes (nutrition, lifestyle habits, eating problems and nutritional support); 3) support for weight monitoring; 4) periodic information for families; and 5) action protocols related to malnutrition risk. The primary outcome measure was loss of autonomy measured in accordance with the ADL and the IADL scales. The secondary outcomes, in turn, were changes in weight, BMI, MNA, and caregiver burden measured on the Zarit questionnaire, and a reduction in the use of health and social services. The mean MNA of the participants at baseline was about 23 points, and the mean MMSE score about 15 points. The one-year intervention significantly improved the MNA in the IG compared to the CG. There were no significant changes in the primary ADL and IADL outcomes, caregiver burden or weight changes between the groups. (Salva et al. 2011)

Nutritional interventions among community-dwelling individuals with AD show that ONSs seem to be beneficial in terms of gaining weight and improving nutritional status (Lauque et al. 2004, Pivi et al. 2011, Salva et al. 2011). Nutritional education targeted at caregivers has been found to help AD subjects to gain weight (Riviere et al. 2001, Pivi et al. 2011, Salva et al. 2011). However, these interventions seemed to have no effect on major outcomes such as ADL or IADL. Furthermore, outcomes related to the quality of life and falls, for example, have not been used in previous studies, and few interventions combine ONSs and tailored nutritional guidance.

Table 7. Nutritional intervention studies among community-dwelling Alzheimer patients

Author	Participants, setting	Outcomes	Intervention	Results
Riviere et al. 2001	N= 227 Non-randomized controlled study Mean age 77 y. in the IG, 75 y. in the CG, Recruited from day hospitals, France, Italy, Spain	Primary outcome: Weight change, other outcomes: MNA, MMSE, ADL and IADL, Cornell scale (mood), Cohen-Mansfield Agitation Inventory (behavioral disorders)	Nine nutritional education lessons targeted at caregivers over one year	Weight increased in the IG and decreased in the CG, but not significantly, differences in MMSE between the IG and the CG (-2.3±0.3 vs.-3.4±0.4, p<0.05), MNA maintained in the IG and decreased in the CG (0.3±2.6 vs - 1.0±3.4, p<0.005)
Lauque et al. 2004	N = 91 RCT Mean age 61 y. in the IG, 65 y. in the CG, risk of malnutrition, Recruited from geriatric wards and day-care centers, France	Primary outcome: Weight change, other outcomes: FFM, MNA, serum albumin, C-reactive protein, ADL, MMSE, dietary intake (24-h recall)	ONSs with 200-500 kcal/daily, 10-12g protein per portion) in addition to normal food intake for three months	Weight (1.57±3.35 kg, p=0.001) and FFM (0.63±1.60 kg, p = 0.001), energy (p = 0.001), and protein (16 ±24g/d, p =0.0001) intake improved, no significant improvement in ADL, MMSE, serum albumin, or C-reactive protein
Planas et al. 2004	N = 44 RCT Mean age 75 y, normal nutrition status Recruited from an Alzheimer Day Centre, Spain	Outcomes: Food intake (3-day food diary), BMI, TSF, MAC, albumin, cholesterol, MMSE	ONSs of 250 ml twice daily, 500 kcal/day, 30 g protein, for six months, with (IG) or without (CG), micronutrient supplementation	Energy intake, TSF and MAC increased in both groups with no difference between the groups, serum cholesterol decreased significantly in the IG compared to the CG (p = 0.025)
Pivi et al. 2011	N = 90 RCT Mean age 75 y., normal nutrition status Recruited from the Neurology clinic, Brazil	Primary outcome: Nutritional status with BMI, AC, AMC, TSF, TP, serum albumin, TLC, MMSE, CDR	6 months, groups included: 1) CG, 2) Education 3) ONS twice daily (680 kcal and 26.6g protein	ONSs increased participants' weight, (p = 0.001), BMI (p = 0.001), AC p=0.002), AMC (p = 0.013) compared to other groups
Salva et al. 2011	N= 946 RCT Mean age 79 y. Recruited from Day Care Centers, Barcelona, Spain	Primary outcome: ADL and IALD, other outcomes: MNA, BMI, weight change, caregivers' burden in accordance with the Zarit score	A teaching and training program directed at both the physician and the main caregiver with a one-year follow-up	The MNA improved in the IG +0.46 (0.09 to 0.83) compared to the CG -0.66 (-0.80 to -0.21); in the CG (p = 0.028), no significant changes in the ADL/IADL and Zarit scores

AC = Arm circumference, ADL = Activities of Daily living, AMC = Arm muscle circumference, BMI = Body mass Index, CG = control group, CDR = Clinical Dementia Rating Scale, FFM = Fat free mass, IADL = Instrumental Activities of Daily Living, IG = intervention group, MAC = Mid-upper-arm circumference, MMSE = Mini Mental state Examination, ONS = Oral nutritional supplement, TLC = Total lymphocyte count, TP = Total Protein TSF = Triceps skinfold, Zarit = caregiver's burden

Nutritional intervention among community-dwelling AD families: a case report

Shatenstein et al. (2008) focused on quasi-experimental pre-post intervention in their Nutrition Intervention Study, which was targeted on community-dwelling, early-stage AD subjects and their primary caregivers in Canada. The aim was to develop and offer tailored nutritional dietary guidance to AD families. The diet of the AD subjects included in the intervention was assessed by means of the FFQ and 24-hour recalls. The guidance was offered by telephone at three-week intervals over a period of six months, and the nutritional plan was sent to the families afterwards. The participants were advised to eat high-quality food to ensure adequate energy and nutrient intake, and they received written nutritional material such as the Canadian Food Guide, recipes, tips for increasing protein and energy intake, and information on adequate fluid intake, exercise and ONSs. (Shatenstein et al. 2008)

The first case Shatenstein et al. (2008) reported in their article was that of a 76-year-old woman (Mrs. R), who suffered from multiple diseases, was on several types of medication, had lost weight during the previous two years, and had a BMI of 20.8 kg/m². She was apathetic and slept during the day, and had a poor appetite. Her energy and nutrient intake was very low at the beginning (energy intake 1,200 kcal, protein intake 29g, calcium intake 251mg, and folic acid 161µg). The nutritional plan encouraged Mrs. R to eat preferred foods, to have a protein source at each meal, to eat snacks and desserts, and to try ONSs. She was also encouraged to have dinner in restaurants with her children as often as possible, because it enhanced her appetite. The intervention concentrated on preventing protein-energy malnutrition, and weight monitoring was also recommended. The intervention helped Mrs. R to gain weight: her BMI at the end was 24.1 kg/m², and she had recovered her appetite. (Shatenstein et al. 2008)

The second case was that of an 82-year-old women (Mrs. M) who had recently been diagnosed as a probable AD sufferer. Mrs. M lived with her sister, who was the main caregiver. Her BMI was very low, at 16.5 kg/m². She had lost nine kilograms after surgery for the removal of polyps and had not regained the weight, and she suffered from constipation. She had a poor appetite and lacked energy. Surprisingly, according to the nutritional assessment her intake of energy and protein intakes was adequate, at 1,857 kcal and 81g daily. However, her intake of vitamin E was low, at 1.4mg. The nutritional plan recommended that Mrs. M should eat several small, nutrient- and energy-dense meals, and more foods that are rich in vitamin E, such as nuts, avocado and olive oil, and fiber. ONSs and weekly weight monitoring were also suggested. Her sister was consistently involved in the intervention, but despite her efforts Mrs. M continued to lose weight, and her BMI at the end was 16.1 kg/m². (Shatenstein et al. 2008)

These case studies describe the intervention strategies, and the challenges facing community-dwelling individuals with AD and their caregivers that should be taken into account in the planning of nutritional interventions for this group. The authors also discuss the strategies that could be used in implementing the tailored guidance, and highlight the importance of caregivers in this process. (Shatenstein et al. 2008)

2.3.5 An overview of studies on dietary supplementation among Alzheimer patients

Specific nutrient deficiencies have been associated with the incidence of AD and its progression in some epidemiological studies (Mi et al. 2013). There has also been research on supplementation in the form of omega-3 fatty acids, antioxidants, vitamin B, and medical foods among community-dwelling individuals with AD. However, the results are inconsistent. Table 8 summarizes the studies focusing on dietary supplementation among community-dwelling older adults, and two non-randomized studies are presented in the text (Nilsson et al. 2001, Lloret et al. 2008).

A Swedish OmegAD study randomized 174 community-dwelling individuals with mild to moderate AD into a 12-week intervention: the IG received omega-3 supplementation containing 1.7g of DHA and 0.6 g EPA, and the CG a placebo (Freund-Levi et al. 2006). No differences between the groups were observed in the primary outcome measure of MMSE, nor on the Alzheimer's Disease Assessment Scale (ADAS - Cog, Rosen et al. 1984). There was a significant reduction in MMSE decline in the subgroup with very mild AD however, with a score of more than 27 points (Freund-Levi et al. 2006). In a Taiwanese RCT study, 23 individuals with mild to moderate AD and 23 patients with MCI were randomized to receive omega-3 supplementation of 1.8 g daily, or olive oil as a placebo. The 24-week intervention had no effect on cognition, although some positive results of omega-3 supplementation on ADAS-Cog were reported among the MCI participants (Chiu et al. 2008). An American study reported no effect on cognition following treatment involving DHA supplementation over 18 months (Quinn et al. 2010). (Table 8)

Galasko et al. (2012) in their double-blind, placebo-controlled study randomized 78 participants with mild to moderate AD into three groups: those given 1) vitamin E (800 IU), vitamin C (500 mg), and α -lipoic acid (900 mg), and 2) coenzyme Q (400 mg) supplements three times daily, or 3) a placebo. After 16 weeks, the vitamin E, vitamin C and α -lipoic acid supplementation (group 1) negatively affected cognition in decreasing the MMSE scores, although it reduced oxidative stress on the brain (Galasko et al. 2012).

Individuals with AD have may have elevated blood-homocysteine levels, which may contribute to the disease pathophysiology via the vascular or neurotoxic mechanism (Nilsson et al. 2001). It was reported in an RCT study of 340 people with AD conducted in the US that high-dose supplementation of folic acid (5 mg/d), and vitamins B12 (1mg/d) and B6 (25mg/d) over an 18-month period managed to improve homocysteine levels those with mild to moderate AD, but had no impact on cognition measured in accordance with the ADAS-Cog (Aisen et al. 2008). It was also found in a Taiwanese study on 89 AD subjects that a 24-week multivitamin supplementation of B6, B12 and folic acid significantly decreased homocysteine levels, but had no effect on the primary outcomes of cognition or ADL (Sun et al. 2007).

A small pre-post intervention study of 28 AD subjects reported that two-month's supplementation of folic acid and vitamin B12 improved cognition measured in accordance

with the MMSE for those with mild to moderate AD and elevated plasma homocysteine levels, but no improvement was observed among those with severe AD and normal plasma homocysteine levels (Nilsson et al. 2001). Lloret et al. (2009) in their Spanish study divided 57 patients with mild to moderate AD into two groups, one receiving vitamin E supplementation of 800 IU daily for six months and the other a placebo. Only 33 participants completed the study. Some of those in the supplementation group benefited in that their oxidative stress markers decreased after the intervention. For others, however, the supplementation did not decrease oxidative stress markers, but even sharply decreased cognitive functioning (Lloret et al. 2009).

There have been some studies on the effect of *medical foods* on AD. Souvenaid®, for example, was developed to improve the synaptic function in the AD brain. It contains omega-3 fatty acids (DHA, EPA), vitamin C, vitamin E, vitamin B6, vitamin B12, selenium, folic acid, choline, uridine monophosphate, and acetyl-L-carnitine, and may synergistically improve the brain's synaptic functioning (Scheltens et al. 2010). Its effectiveness has been studied in RCT studies among those with mild AD. Scheltens et al. (2010), for example, randomized 225 drug-naïve AD subjects into a 12-week trial, and significant improvement in the verbal-recall task was noted in the IG compared to the CG ($p = 0.02$). However, no effect was observed in other outcomes such as ADAS-Cog, ADL, or quality of life. However, the secondary analyses reported in Kamphuis et al. revealed a significant treatment effect on ADAS-Cog ($p = 0.046$) among those with high baseline ADAS-Cog vs the CG, but no effect on those with low ADAS-Cog vs the CG at baseline (Kamphuis et al. 2011b). An increase in BMI in the IG compared to the CG was observed in the same study (Kamphuis et al. 2011a). Souvenaid® was further tested in a double-blind, multicenter RCT among 259 participants with mild AD recruited from several AD centers, in which the IG received Souvenaid®, and the CG an isocaloric placebo product for 24 weeks. The NTB memory domain Z score revealed differences between the groups (Scheltens et al. 2012). A large RCT study among 579 subjects with mild to moderate AD reported no beneficial effect of Souvenaid® on cognition measured in accordance with ADAS-Cog after a 24-week intervention (Shah et al. 2013). Souvenaid® has been reported to be well tolerated up to 48 weeks, with a low level of adverse effects (Olde Rikkert et al. 2015). (Table 8)

Table 8. An overview of RCT studies investigating nutritional supplementation and medical food among older adults with Alzheimer's disease

Author	Participants, setting	Outcomes	Intervention	Results
Nutritional supplementation studies				
Freund-Levi 2006	N = 174 Mean age 73 years Mild to moderate AD Sweden	MMSE, ADAS-Cog CDR	Omega-3 fatty acids of 1.7g of DHA, 0.6g EPA vs placebo 12 weeks	No significant differences in MMSE, ADAS-Cog, significant reduction ($p < 0.05$) in MMSE decline in the subgroup ($n = 32$) of those with MMSE > 27
Sun et al. 2007	N = 89 Mean age 75 years Taiwan	ADAS-Cog, ADL	Multivitamin supplementation (B6, B12, folic acid) 26 weeks	No effect on ADAS-Cog or ADL, Significant difference in serum homocysteine concentration in IG vs CG ($p = 0.008$), and serum B12 ($p < 0.001$) and folic acid concentrations ($p = 0.012$)
Aisen et al. 2008	N = 340 Mean age 76 years Mild to moderate AD USA	ADAS-Cog, MMSE, CDR-SOB, ADAS-Cog	Folic acid 5 mg, vitamin B12 1 mg and B6 vitamin 25mg / daily vs placebo 18 months	No effect on ADAS-cog, or other outcomes, homocysteine levels decreased significantly in the IG compared to the CG, $p < 0.001$
Chiu et al. 2008	N = 23 Mean age 75 years Mild to moderate AD, and MCI Taiwan	CIBIC-plus, ADAS- Cog, MMSE	Omega-3 supplementation 3 capsules twice daily, total of 1080mg EPA and 720 mg DHA, 24 weeks	Significant difference in CIBIC-plus in the IG vs the CG $p = 0.008$. No effects on ADAS-Cog or MMSE, significant improvement in ADAS-cog in the IG vs the CG with MCI patients ($p = 0.03$)
Quinn et al. 2010	N = 295 Mean age 76 Mild to moderate AD USA	ADAS-Cog, CDR, MMSE, ADCS-ADL	DHA 2g/day vs placebo 18 months	No treatment effect on outcomes
Galasko et al. 2012	N = 78 Mean age 73 years Mild to moderate AD USA	CFS biomarkers, MMSE, ADCS-ADL	1) Vitamin E 800 IU, vitamin C 500mg, α - lipoic acid 900 mg daily, 2) Coenzyme Q (400 mg) three times daily, 3) Placebo 16 weeks	Group 1 affected via a decline in MMSE
Medical food studies				
Scheltens et al. 2010	N = 225 Mean age Drug-naïve AD patients	WMS-r, ADAS-Cog, WMS-r delayed verbal recall, NPI, ADCS-ADL	Souvenaid® vs. isocaloric placebo (125 mL daily dose) 12 weeks	Significant improvement in the VMS delayed verbal task in the IG compared to the CG ($p = 0.02$), no effect on other outcomes
Kamphuis et al. 2011b	N = 225 Mean age 74 Mild AD, MMSE 20–26	WMS-r, ADAS-Cog	Souvenaid® vs. isocaloric placebo (125 mL daily dose) 12 weeks + 12-week extension period	Significant treatment effect on ADAS-Cog ($p = 0.046$) among those with high baseline ADAS-Cog vs the CG, no effect on those with low ADAS-Cog vs the CG at baseline

Continues				
Author	Participants, setting	Outcomes	Intervention	Results
Scheltens et al. 2012	N = 259 Mean age 74 Mild to moderate AD	NTB NTB memory domain	Souvenaid® vs isocaloric placebo 24 weeks	Improvement in the NTB memory domain Z score in the IG vs. the CG (p = 0.023), the effect on the total NPB Z score was not significant (p = 0.053)
Shah et al. 2013	N = 579 Mean age 77 Mild to moderate AD	ADAS-Cog	Souvenaid® vs isocaloric placebo 24 weeks	ADAS-Cog declined in both groups, no significant group difference, no difference in adverse events
Olde Rikkert et al. 2015	N = 201 Mean age 74 Mild to moderate AD	Safety and product adherence	Souvenaid® 48 weeks	Well tolerated with a low level of adverse effects, high intake adherence (96%)

ADCS-ADL = 23-item Alzheimer's disease cooperative study-ADL, CDR-SOB = Clinical Dementia Rating sum of boxes, CIBIC-Plus = Clinician's Interview-Based Impression of Change Scale, CFS = cerebrospinal fluid, WMS-r = Memory Scale-revised, Memory scale -verbal recall test of the Wechsler, NTB = Neuropsychological Test Battery

2.4 THE CAREGIVER'S ROLE IN NUTRITION IN ALZHEIMER FAMILIES

2.4.1 The caregiver's role in Alzheimer families

Most people with AD need care either in institutions or at home. Both behavioral and psychological symptoms and functional difficulties increase the caregiver's burden (Bergvall et al. 2011), and consequently the cost of the disease (Beeri et al. 2002): the level of ADL skills is the most reliable predictor of the societal costs of AD (Gustavsson et al. 2011). Many people with AD are looked after at home by their spousal caregiver, especially during the early stages (Poysti et al. 2012). The caretaking tends to be comprehensive, and may cause psychological distress, affective symptoms, and physical and financial hardship (Pinquart & Soderksen 2003, Iavarone et al. 2014).

Chronic stress is assumed to affect the immune system of older caregivers, and to increase their disease risk and mortality (Glaser et al. 2001, Gouin et al. 2008). Several studies report that caregivers are more highly exposed than non-caregivers to illnesses such as high blood pressure, metabolic syndrome, hyperlipidemia, diabetes, cardiovascular disorders and coronary heart disease, and infectious diseases (Kiecolt-Glaser et al. 1991, Shaw et al. 1999, Dauphinot et al. 2015). It has also been found that spousal caregivers are more likely to suffer from loneliness, depression and anxiety than non-caregiving spouses (Beeson 2003, Cooper et al. 2007).

2.4.2 Caregivers and nutrition

Eating and food have social meanings and functions. Keller et al. (2006) found in their qualitative study that caregivers in AD families experienced meal times as social and enjoyable, and meal-time rituals helped the AD family members to remain emotionally connected even in cases when normal discussion was no longer possible. Of these caregivers, 65 percent were spouses and 35 percent were offspring (Keller et al. 2006). According to another qualitative study (Genoe et al. 2012), meal times in AD families give space for the honoring of individual and collective identity, staying connected, and adapting to and accepting life. Although mealtimes are considered important, they may also generate stress in AD families because of various changes in eating behavior in the sufferer, such as difficulties in using utensils, agnosia, changed food preferences, difficulties in eating out and resisting behavior, decreased food intake and diversity, and decreased autonomy (Silva et al. 2013). The caregiver's burden may also increase the likelihood of feeding difficulties among AD family members (Riviere et al. 2002).

The increased stress and comorbidities may put caregivers at an increased risk of malnutrition. Rullier et al. (2014) showed in their French cross-sectional study that 32 percent of caregivers were at risk of malnutrition, and five percent were malnourished. The

higher prevalence of neuropsychiatric symptoms and dependency among the AD subjects in these families was associated with the caregiver's lower MNA score (Rullier et al. 2014).

2.4.3 Gender differences in caregiving and nutrition

Baker & Robertson (2008) conducted a systematic review of studies investigating gender differences in caregiving. Gender differences in coping with dementia were reported in 19 studies, in the majority of which women experienced more distress and used more services than men. However, four studies reported no gender differences (Baker & Robertson 2008). It was found in a Finnish cross-sectional study of 335 couples comprising an AD sufferer and a spousal caregiver that male caregivers experienced significantly less stress, even if they had more comorbidities and their wives were at a more severe stage of AD (Poysti et al. 2012).

Women have traditionally been in charge of food-related activities in the aging population, and cooking is considered to be 'women's work' - as reported in a Finnish qualitative study investigating men's attitudes toward cooking (Roos et al. 2001). Women also tend to continue to engage in household activities long after receiving an AD diagnosis, and men in this situation start to take responsibility for household activities step by step (Genoe et al. 2012). It is suggested in some studies that men tend to consume less fruit and vegetables than women, indicating a poorer diet (Bates et al. 1999, Baker & Wardle 2003). Bates et al. (1999) further reported that men tended to be less interested in nutritional issues than women. According to some studies, a lack of nutritional knowledge and poor cooking skills explain the poorer diet (Baker & Wardle 2003, Hughes et al. 2004). It has also been reported that men in families with an AD spouse tend to worry about managing household activities (Fjellstrom et al. 2010).

The growing number of older adults and AD families means that more men are becoming caregivers (Poysti et al. 2012). Gender differences seem to be present in both caregiving and nutrition, but thus far there are no studies investigating the association between the caregiver's gender and nutrition in AD families.

2.5 A SUMMARY OF THE LITERATURE

Energy requirements decrease with age due to diminished muscle mass and exercise, but the need for nutrients remains stable or may even increase. People with AD are especially prone to nutritional problems, and unintentional weight loss and malnutrition are common among them. Nutritional problems are associated with poor outcomes such as AD progression, the need for institutionalized care, a diminished quality of life, morbidity, and mortality.

Some epidemiological studies report adequate mean intake of energy and nutrients among older adults. However, it is a highly heterogeneous group, and it is reported in several studies

that a large proportion of participants fail to receive adequate amounts of several essential nutrients. Thus, the risk of malnourishment is common in older populations.

Many AD patients live in their own homes and are taken care of by older spousal caregivers, who may have multiple comorbidities, and also be at an increased risk of malnutrition. Caregivers tend to be responsible for food management in AD families. Women have traditionally assumed this role, but in recent years the number of male caregivers has increased. Some studies indicate that men in this age group may have problems managing food-related activities, and they may also have a poorer diet than women.

Some nutritional interventions among AD patients have produced promising results in terms of weight and nutritional status, and ONS have contributed to weight gain among those with weight loss. However, thus far no randomized, controlled studies have investigated the effect of tailored nutritional guidance on nutrient intake, quality of life, and the risk of falls.

3. THE AIMS OF THE STUDY

The objective of this study is to investigate nutrition among older adults with AD and their spousal caregivers in the light of recommended levels, separately in men and women, and further to examine the effects of tailored nutritional guidance on the weight of individuals with AD, as well as the feasibility of nutritional guidance among AD couples.

The specific aims of the study were:

1. To report the nutritional status and nutrient intake of community-dwelling individuals with AD and their spousal caregivers, and to compare the intake to recommended levels (Articles I, II)
2. To study the association of the caregiver's gender with nutrient intake in AD families (Article II)
3. To investigate the effect of tailored nutritional guidance on weight, nutritional status, nutrient intake, quality of life, and falls among community-dwelling individuals with AD during a one-year intervention (Article III)
4. To assess the feasibility of the intervention in qualitative terms (Article IV)

4. SUBJECTS AND METHODS

4.1 The subjects and the study design

This study was conducted in 2009-2012 as part of a Nutrition Project for the Society of Memory Disorders in Finland. A randomized, controlled design was used, and the study explored the effectiveness of tailored nutritional guidance given to AD-affected couples. The participants were recruited from the Central Drug Reimbursement register of the Social Insurance Institution of Finland (Kela) in 2010, and included couples comprising an AD sufferer living at home with his or her elderly spousal caregiver in the greater Helsinki area. To qualify for drug reimbursement the partner concerned had to have a confirmed AD diagnosis according to the NINCDS-ADRDA Alzheimer's criteria (McKhann et al. 1984). A letter was sent via Kela to a sample of 643 couples fitting the above description. Those expressing interest in the study replied to the letter, and were contacted by the nurse involved in the study to ensure that they fulfilled the inclusion criteria. Figure 3 presents the flow chart of the study.

The inclusion criteria were:

- The age of the AD spouse was 65 or more
- The AD patient was living at home with his or her elderly spouse
- The couple lived in the Greater Helsinki area
- The couples were able to communicate in the Finnish language
- The couples were able to use a taxi to travel to the study assessments
- The couples were able to stand on the scales
- The couples did not have a terminal disease, and had an estimated life expectancy of at least half a year (confirmed by medical records)

The participants who fulfilled the above criteria were invited to the first study meeting and assessments in Simonkylä Day Care Center, Vantaa. During the first assessment visit both the AD patient and his or her spousal caregiver were assessed for nutrition, cognition, functional ability, quality of life and caregiver's burden.

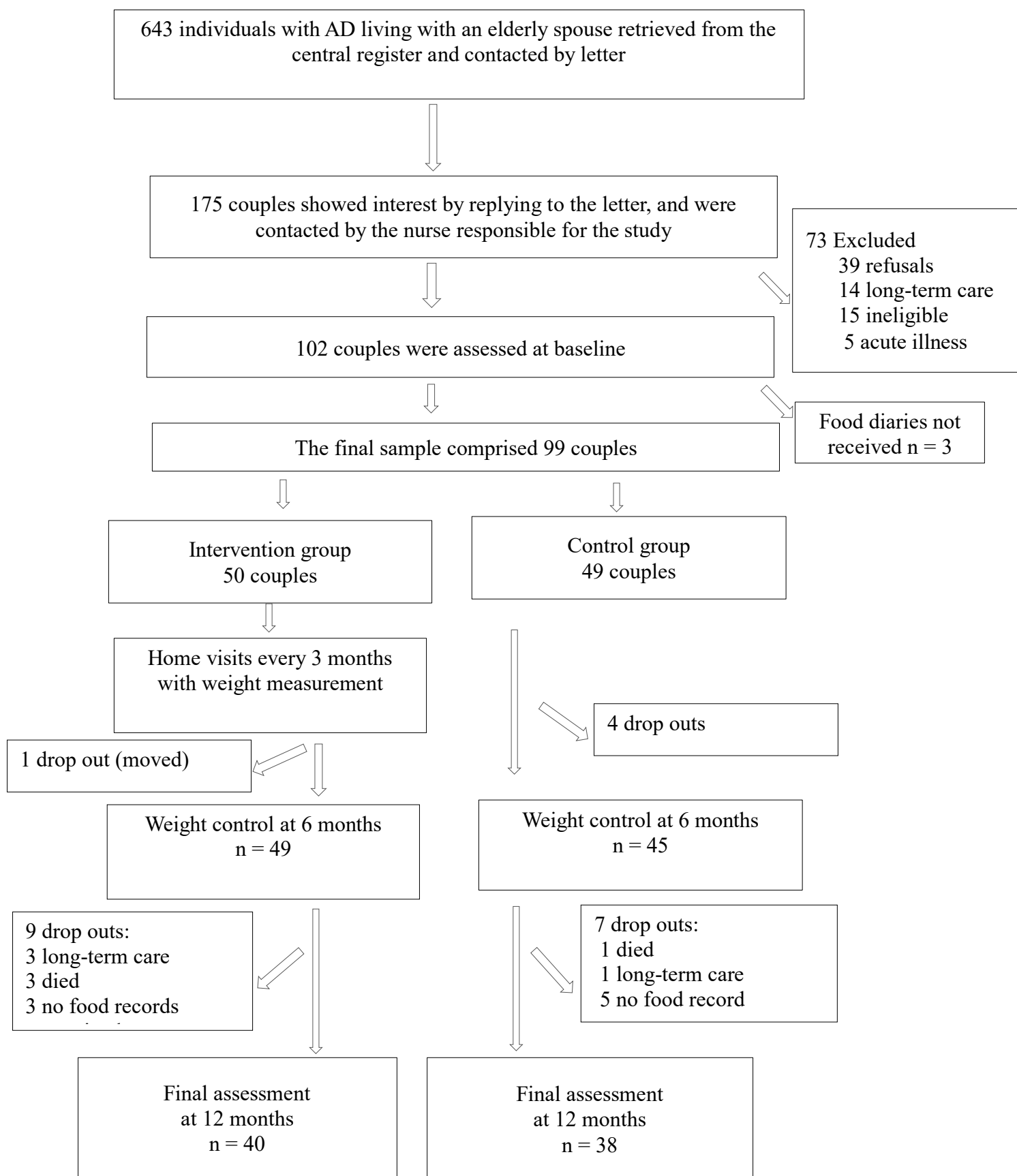


Figure 3. The flow chart of the study

4.2 Measurements

The study participants underwent detailed assessments. The demographics (e.g. age, gender, education, and income) were reported on both those with AD and their caregivers. Diseases and medications were confirmed from the medical files. The weight and height of the participants were measured at baseline, and their BMI was calculated by dividing their weight in kilograms by the square of their height in meters. The trained nurse responsible for the study carried out all the measurements at the beginning and the end of it. The measurements are described below.

MNA and food diaries were used to measure nutrition. The full MNA was administered to all participants, even if they had scored enough points during the screening. Food diaries were collected over three days when the participants were following their usual diet, and were provided by the spouses. The nutritionist gave spoken and written instructions to caregivers on how to record their spouse's dietary intake during the first assessment session. They were instructed to note the amounts of drink and food consumed during the three days on the food-diary sheet, and were given cups to measure the respective amounts. The participants were also advised to use trademarked food items to ensure the right nutritional content. After completing the food diaries the caregivers sent them to the nutritionist, who checked all the entries by telephone. The nutritionist then calculated the intake of energy and nutrients in accordance with the Nutrica program, which was created and updated by the Social Insurance Institution of Finland (Rastas et al. 1997). The program includes a database of 1,300 foods and 700 ingredients, and several trademarked food items. It shows energy and nutrient intake in numbers and graphics, presenting nutrient intake compared to recommended levels, which was feasible in the education process (Rastas et al. 1997). The same person recorded the food diaries at the beginning and at the end of the study to ensure consistency in the recording process.

The MMSE test measures global cognition (Folstein et al. 1975). It comprises a 30-point questionnaire based on seven dimensions of cognition: orientation to time and place, attention and concentration, registration, recall, language, and visual construction (Folstein et al. 1975). An MMSE score of 0-10 (12) indicates severe dementia, 10 (12) – 18 average dementia, 18 (20) – 24 mild dementia, and 24-30 normal cognition (Folstein et al. 1975). The MMSE may be used for screening, but it is not a diagnostic tool: depression, dysphasia or delirium, for example, may impair the score (Tombaugh & McIntyre 1992). A high educational level seems to help people to achieve a good MMSE score despite having AD (Mulligan et al. 1996).

The CDR divides demented people into four categories according to the severity of their condition (Hughes et al. 1982). It combines the assessment of cognitive and daily physical functioning in six domains: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and the need for personal care (Hughes et al. 1982). Each domain is evaluated on a five-point scale (0, 0.5, 1, 2, 3). The memory category determines the basis of

the global CDR value, which the other domains may decrease or increase by one step (Hughes et al. 1982): A CDR rating of 0 denotes no dementia, 0.5 possible dementia, 1 mild dementia, 2 moderate dementia, and 3 severe dementia. Evaluators may interview the spousal caregiver and the AD subject to obtain the CDR value (Hughes et al. 1982).

The 15D questionnaire was developed to measure health-related quality of life (HRQoL) (Sintonen 2001). It is multi-dimensional, self-administered, and includes physical, emotional and social components. The 15D score varies between zero and one, and high reliability has been shown (Sintonen 2001). It is a generic measure, and can be evaluated by the person concerned as well as by a proxy (Sintonen 2001).

The IADL test was used to measure the participants' need for help in their daily activities. Developed and validated by Lawton & Brody (1969), the test contains eight questions that examine an individual's ability to use the telephone, go shopping, carry out cooking, housekeeping and laundry tasks, use transportation, deal with their medication, and manage financial matters. This test score was used because it indicates the cognitive ability of participants to perform the various tasks. The ability to perform the tasks is not associated with educational level or gender (Lawton & Brody 1969).

The Zarit Burden Scale measures the caregiver's experienced burden by means of a self-report questionnaire (Zarit et al. 1980). The scale with its 29 questions was originally developed to estimate the stress factors, but it was modified in 1983 and now includes 22 questions. The choice of questions was based on clinical experience and previous studies. Each question is rated on a five-point scale ranging from 0 (never) to 4 (nearly always). The maximum number of points is 88, a higher score indicating a heavier burden. The following cut-off points may be used: 0-20 indicating a minor or no burden, 21-40 a mild or average burden, 41-60 a medium or strong burden, and 61-88 a heavy burden (Zarit et al. 1980). A short version comprising 12 questions has been developed for screening purposes, and the results of this short version and the longer version, which was used in this study, are comparable (Bedard et al. 2001). Van Durme et al. (2012) showed in their review that the Zarit Burden Interview is feasible for researchers and clinicians to use, and is well validated.

Falls were retrieved from the 'fall diaries' kept by the spousal caregivers, which in this study were checked at the couple's home during the six-monthly visit, and at the end of the intervention. The fall rates of participants in the IG and CG were compared at the end of the intervention.

The Charlson comorbidity index, which takes into account the number and severity of comorbid diseases, was calculated for each participant from the background information. The index was developed in a cohort of 559 medical patients. One-year mortality rates were "0" 12%, "1-2" 26%, "3-4" 52%, and ≥ 5 85%. The index was tested in the second cohort of 685 patients during a ten-year follow up, and an increased comorbidity index score indicates an

increase in mortality. Severity is coded as 0 absent, 1 = not ill, 2 = mildly ill, 3 = moderately ill, 4 = severely ill. (Charlson et al. 1987)

4.3 Randomization

A computer-based randomization process was implemented after the investigators had received and saved the food diaries. The person in charge of the randomization was not involved in assessing the participants.

4.4 Intervention

The IG received tailored nutritional guidance at their homes, and the participants in the CG received written guidance on nutrition for older adults. At the end of the intervention the written feedback from the food diaries was offered to members of the CG, who were also invited to the final seminar.

The one-year intervention consisted of assessment-based, tailored guidance at the couples' homes. The nutritionist arranged the first home visit with the couples concerned shortly after the randomization. During this visit she discussed nutritional issues in general and gave the couples the results from their own food records. The themes discussed included grocery shopping, cooking, food habits, and food preferences, as well as attitudes towards nutrition and healthy eating. The nutritional guidance was participant-centered and both the partner with AD and the spousal caregiver were involved. It was focused on the caregivers, however, because in most cases they were responsible for the nutrition-related activities in the families. The guidelines were based on healthy dietary principals according to Finnish Nutritional Recommendations (National Nutrition Council 2005) and Finnish Nutritional Recommendations for older adults (National Nutrition Council 2010), taking into consideration each couple's dietary habits and food preferences.

The nutritionist wrote an individual nutritional care plan (NCP) for each participant, based on information from the first assessment, the food records and the discussions during the first visit, and mailed it to the couples shortly afterwards. The plan started with positive feedback on each participant's diet. It gave information about energy and nutrient intake compared to the recommendations, and practical suggestions for improving the diet. Tailored guidance was given according to the couples' individual needs: those experiencing weight loss were given information about energy-rich food, and those with a medium or high BMI were advised to maintain their weight and to do more exercise. All the participants were also encouraged to exercise as far as their own health and functionality allowed. Table 9 lists the main elements of the intervention and the means by which it was implemented.

The themes written down in the NCP were discussed in the following visits: the participants were asked what they thought about it, whether they had benefited from the suggestions and

if they had been able to make changes in their diets. If the guidance was not suitable for them other suggestion were given, and the nutritionist also gave dietary feedback.

The nutritionist visited the couples at least once every three months, and measured their weight on a portable scale. The number of visits was tailored to the couples' needs, and those who needed more support were visited more often up to a maximum of eight times. Given that the IG couples were seen at least every three months, the nutritionist was well aware of what was going on in the families. ONSs were also supplied to participants who could not improve their diet based on food intake.

The nutritional intervention reflected benefits reported in earlier studies. The main elements included information about AD-related weight and weight loss (Gillette-Guyonnet et al. 2007), sufficient energy, protein and nutrient intake (Shatenstein et al. 2008), the use of ONSs (Lauque et al. 2004, Hanson et al. 2011), mealtimes and nutrient-dense snacking (Zizza et al. 2007), vitamin D supplement 20 µg (Bischoff-Ferrari 2009), recommendations for exercise (Pitkala et al. 2013), and housekeeping and cooking.

Table 9. The main elements of the intervention and its implementation based on theories of constructive learning

THE MAIN ELEMENTS OF THE INTERVENTION		THE MEANS OF IMPLEMENTATION
<ul style="list-style-type: none"> - Tailored guidance on weight or unintentional weight loss - Sufficient energy, protein and other nutrient intake - Vitamin D supplementation - Use of oral nutritional supplements (ONSs) - Exercise - Housekeeping and cooking 	<p>Constructive learning theory</p> <p>Reflection</p>	<ul style="list-style-type: none"> - Home visits - Tailored nutritional care plan, NCP - Personal discussions - Booklet on good nutrition for older adults - Brochures about sources of protein, calcium and vitamin D, and exercise - ONSs when needed

The guidance was implemented via 1) home visits and personal discussions (Bernstein et al. 2002), 2) a tailored written nutritional care plan (NCP) (Shatenstein et al. 2008), 3) a booklet on healthy nutrition for older adults with practical examples, 4) brochures with photos of good sources of protein and calcium, 5) a brochure on vitamin D supplement 20 µg daily, and 6) a booklet on exercise. 7) The participants also had the opportunity to call the nutritionist and to take part in a group meeting aimed at enhancing peer support and reinforcing the nutrition message (Sahyoun et al. 2004).

The nutritionist took a participant-centered approach in her discussions with the couples during the home visits. The main themes included the findings from the food diaries, and food-related issues such as appetite, cooking and grocery shopping. The nutritionist also gave practical suggestions for dietary improvement, simultaneously listening to the participants'

wishes and ideas. The aim was to empower the participants to make positive changes in their nutrition habits.

Outcome measures

The primary outcome measure in the RCT study was the participants' weight change, and the secondary measures were nutrient intake, nutritional status, health-related quality of life, and falls (Table 10).

Table 10. The outcome measures used in the RCT study

Primary outcome measure	
Weight change	Measured every three months in the intervention group on a calibrated scale, and in the control group after 6 months
Secondary outcome measures	
Nutritional status	Mini Nutritional Assessment (MNA) -test (Vellas 1999)
Nutrient intake	3-day food diaries (Thompson & Bayers 1994)
Health-related quality of life	15D = Health-related quality of life (Sintonen 2001)
Falls	Caregiver-reported fall-diaries (Hannan et al. 2010)

4.6 Data handling and statistical analysis

The data was collected during 2010-2012 and was saved in the ACCESS database (Microsoft Office 2010).

The power calculations for the intervention study were based on an earlier study, the expected weight change in AD patients with a standard deviation of 3.6 (Riviere et al. 2001), and a type-1 error of five percent. At the power of 80% and an expected weight difference of 2 kg between individuals in the intervention and control groups, the aim was to randomize 50 persons for each group to show a difference. The SPSS and the STATA 12.1 statistical package (StataCorp LP, College 20 Station, TX, USA) were used for the statistical analyses.

The baseline gender differences between the IG and the CG were compared by means of the χ^2 -test or Fisher's exact-test for categorical variables. The student t-test or the Mann Whitney *U*-test was used to compare the continuous variables depending on their normality. Bootstrap-type covariance analysis (ANCOVA) was used to investigate the association between the caregiver's gender and nutrient intake, with age and MMSE as covariates. In the case of the treatment's effect on outcome measures (Table 10), bootstrap-type analysis of covariance (ANCOVA) was used, and the analyses were adjusted to baseline gender, age, MMSE and BMI. Multivariate forward stepwise logistic regression analysis was used to determine the characteristics associated with protein intake.

Cohen's paired-samples method (mean baseline scores minus mean follow-up scores, divided by the pooled standard deviation) was used to calculate the effect size ("d") in the analyses of gender differences and the effectiveness of the intervention on nutrient intake (Cohen et al. 1988). An effect size of 0.20 was considered small, 0.50 was medium, and 0.80 was large. The confidence Intervals (CIs) for the effect sizes were obtained by means of bias-corrected bootstrapping (5000 replications).

A grounded-theory approach was adopted for the qualitative study. Thematic content analysis was used to describe the feasibility of the tailored nutritional guidance, and the positive elements and challenges the intervention faced. The data for the qualitative analysis included the nutritionist's field notes and the participants' responses to the open-ended questions in the feedback questionnaires. To start with, the data was read several times to find the themes. The key points were marked as a series of codes and grouped further into categories. Constant comparison was used to compare each theme to the rest of the data (Silverman 2000).

Table 11 summarizes the articles comprising this dissertation, including the aims, participants, measurements, and statistical methods.

Table 11. An overview of the four articles included in the dissertation

	Article 1 Cross-sectional	Article 2 Cross-sectional	Article 3 Randomized, controlled trial	Article 4 Qualitative analysis
Aim	To present the baseline results concerning the study participants	To study the association between the caregiver's gender and nutrient intake	To investigate the effectiveness of tailored nutritional guidance	To describe the feasibility of an intervention, the challenges and opportunities
Participants	Baseline data N =99 couples	Baseline data N = 99 couples	AD patients who completed the final assessments N= 78 (40 in IG, 38 in CG)	Couples who completed the intervention N=40 IG couples
Measurements	MMSE, CDR, MNA, nutrient intake, IADL, Zarit burden scale	Nutrient intake, MNA, MMSE, Charlson comorbidity index, Zarit burden scale	Weight change, nutrient intake, 15D, rate of falls	Nutritionists' field notes, feedback questionnaires provided by the couples at the end of the intervention.
Statistical methods	Khii ² -test, t-test, Mann Whitney U-test	Bootstrap-type covariance	Bootstrap-type covariance	Grounded theory, thematic content analysis

CDR = Clinical Dementia Rating Scale, CG = control group, IADL = Instrumental Activities of Daily Living, IG = Intervention group, MMSE = Mini Mental State Examination, MNA = Mini Nutritional Assessment measuring nutritional status, Zarit burden scale measuring caregiver's burden, 15D = Health-related quality of life

4.6 Ethical questions

The Ethics Committee of the Helsinki University Central Hospital approved this study. The participants received both written and verbal information, and they were invited to ask questions about the study before the procedures started. All the participants gave some form of informed consent: if the spouse with AD was unable to give his or her informed consent, his or her caregiver did so on his or her behalf. The data is saved in a password-protected secure file, and data without identification numbers has been created for each separate work (Article).

5. RESULTS

5.1 Baseline characteristics (Article 1)

Table 12 presents the baseline characteristics of the study participants. Females represented 68 percent of the caregivers. The mean age of those with AD was 77.4 years (SD 5.6), and of the caregivers it was 75.2 years (SD 7.0); in terms of educational level, 29 percent and 20 percent, respectively had fewer than eight years of schooling. The mean MMSE score among those with AD was 19.3, and the majority of them were in the mild to moderate stage of the disease according to the CDR scale. (Table 12).

Table 12. The baseline characteristics of the study participants

	Those with AD N=99	Spousal caregivers N=99
Mean age, (SD)	77.4 (5.6)	75.2 (7.0)
Males, (%)	69	31
Education < 8 years, (%)	29	20
Mean MMSE, (SD)	19.3 (5.6)	27.5 (2.2)
CDR, %		
0.5	20	-
1	36	
2	36	
3	7	
MNA, %		
< 17 points	-	-
17-23.5 points	44	16
> 23.5 points	56	84
Weight, mean (SD)		
Females	69.8 (13.8)	67.9 (10.4)
Males	77.6 (10.9)	77.6 (9.8)
Mean BMI, (SD)	26.3 (3.8)	26.6 (4.1)
The BMI classes, %		
< 20	3	4
20-24	23	26
24-29	53	46
>29	21	23
Mean IADL, (SD)	3.6 (2.2)	7.9 (0.5)
Mean number of medications (SD)	5.6 (2.6)	3.9 (2.4)
Charlson comorbidity index, mean (SD)	1.98 (1.2)	1.18 (1.5)
Mean 15D, (SD)	0.761 (0.119)	0.863 (0.088)
Mean Zarit score (SD)	-	29.3 (15.8)

BMI = Body mass index = weight (kg) / height (m)², CDR = Clinical Dementia Rating Scale: 0.5 possible dementia, 1 mild dementia, 2 moderate dementia, 3 severe dementia, Charlson comorbidity index, with higher score indicating more comorbidities, IADL = Instrumental Activities of Daily living, score 1 to 8, with higher score indicating better functioning, MMSE = Mini-Mental State Examination; 24-30 normal cognition, 18-24 mild dementia, 10-18 average dementia, 0-10 severe dementia, MNA = Mini Nutritional Assessment; < 17 points malnourishment, 17-23.5 points risk for malnutrition, >23.5 points good nutritional status, SD = standard deviation, Zarit = caregiver burden; 0-20 indicates minor or no burden, 21-40 mild or average burden, 41-60 medium or strong burden, and 61-88 high burden. 15D = Health-related quality of life; 0 = indicating poor quality of life, 1 = indicating good quality of life

According to the MNA, 44 percent of those with AD and 16 percent of the spousal caregivers were at risk of malnutrition, whereas 56 and 84 percent, respectively, had a good nutritional status. None of participants were malnourished. Only three percent of those with AD, and four percent of the spouses had a BMI of less than 20, and the mean BMI was about 26 in both groups. (Table 12)

5.2 Energy and nutrient intake at baseline (Articles 1 and 2)

Table 13 presents the mean energy and nutrient intake levels for the most relevant nutrients, separately for men and women with AD and the spousal caregivers. As the table shows, there was considerable heterogeneity in nutrient intake.

Table 13. The mean intake levels and ranges of energy and nutrients among those with AD and their spouses

	Those with AD		Spouses	
	Men n = 68	Women n = 31	Men n = 31	Women n = 68
Energy, kcal	1897 (1012-3016)	1313 (520-1774)	1605 (992-2680)	1536 (604-2594)
Protein, g	80 (40-143)	58 (18-90)	70 (32-124)	67 (18-117)
Protein, g/kg	1.04 (0.5-1.74)	0.86 (0.27-1.54)	0.93 (0.43-1.67)	1.0 (0.29-1.81)
Vitamin A, RE,	1223 (408-4993)	808 (253-2547)	1127 (262-5492)	1045 (233-3812)
Vitamin E, mg	10.9 (4.5-24)	6.4 (2.2-18)	8.5 (3.4-21)	9.5 (2.5-30)
Vitamin C, mg	93 (22.2-268)	54 (5.7-146)	63 (7.9-212)	84 (15-201)
Vitamin D, µg	12 (1.6-61)	7 (1.4-19.1)	8 (1.6-24)	10 (1.3-31)
Vitamin B1, mg	1.2 (0.6-2.2)	0.86 (0.3-1.6)	1.1 (0.5-1.9)	1.1 (0.3-2.2)
Vitamin B2, mg	1.9 (0.8-3.5)	1.5 (0.7-2.9)	1.8 (1.0-4.1)	1.6 (0.6-3.0)
Vitamin B12, µg	7.7 (1.4-42)	4.7 (1.3-10)	5.9 (1.7-19.7)	6.2 (0.9-21)
Folate, µg	258 (125-438)	180 (57-307)	219 (96-386)	226 (63-443)
Calcium, mg	1027 (301-2266)	826 (247-1693)	945 (413-2005)	859 (347-1693)
Iron, mg	10.8 (5.1-17.7)	7.8 (2.9-13.8)	10 (4.3-178)	9 (3.4-17)
Selenium, µg	83 (46-152)	54 (13-110)	70 (31-117)	68 (18-138)
Zinc, mg	12.1 (5.7-21)	8.9 (3.4-15)	11 (6.3-20)	9.9 (3.2-16)

The mean energy intake of those with AD was 1,897 kcal among the men and 1,313 kcal among the women. The respective figures for the spousal caregivers were 1,605 and 1,536. The mean protein intake in grams and in grams per kilogram of bodyweight among those with AD was 80g and 1.04g for the men, and 58g, and 0.86g for the women. The respective figures for the spousal caregivers were: 70g and 0.93g, and 67g and 1.00g. (Table 12)

The percentage of participants with a lower-than-recommended intake of several nutrients was high: the majority of the women and about half of the men with AD had a protein intake of less than 1g/kilogram. There were also high percentages in both groups with low levels of vitamins C and E, and iron and folate. The folate intake of the majority of the participants was less than adequate. (Figure 5)

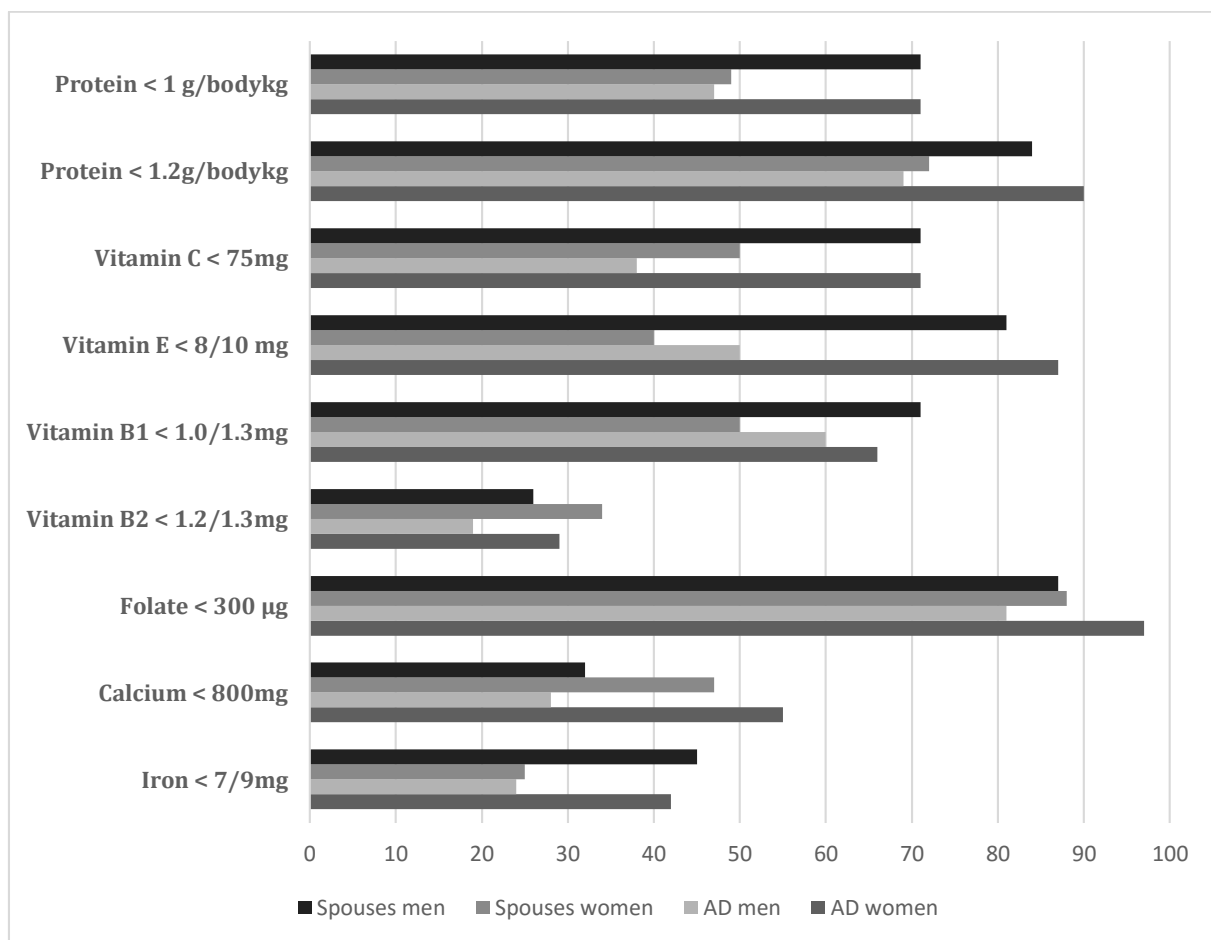


Figure 5. The proportions (%) of participants who received less than the recommended level of nutrients

A forward regression model for poor protein intake (<1.0g/body kg) was built to explore which variables were associated with protein intake at baseline. Among those with AD, when age, gender, education, MMSE, CDR, IADL, medications, Charlson comorbidity index, and income were entered into the model as independent variables, the female gender ($p=0.007$)

and Charlson (0.007) were statistically significant associates with a poor protein intake. For the spouses, when age, gender, education, MMSE, CDR, IADL, medications, Charlson comorbidity index, income, and the Zarit score were entered as independent variables, the male gender (0.024) and a poor income (0.016) were statistically significantly associated with a poor protein intake. (unpublished results)

5.3 The caregiver's gender and nutrition (Article 2)

The intake of energy and nutrients was significantly lower in the families with a male as opposed to a female caregiver. The interaction between the caregiver's gender and the intake of several nutrients (vitamins C, E, D, and folate) persisted, but was not as clear in the case of calcium.

There were some gender differences in baseline characteristics. The male caregivers were older than the female caregivers. The mean age of the male caregivers was 77.4 (SD 7.1), compared to 74.2 (SD 6.7) years, $p=0.030$ among the females, and they had a higher comorbidity index (males 1.7 (SD 1.8) points versus females 0.9 (1.2) points, $p = 0.049$). The analyses were therefore adjusted for these variables, but the result remained significant.

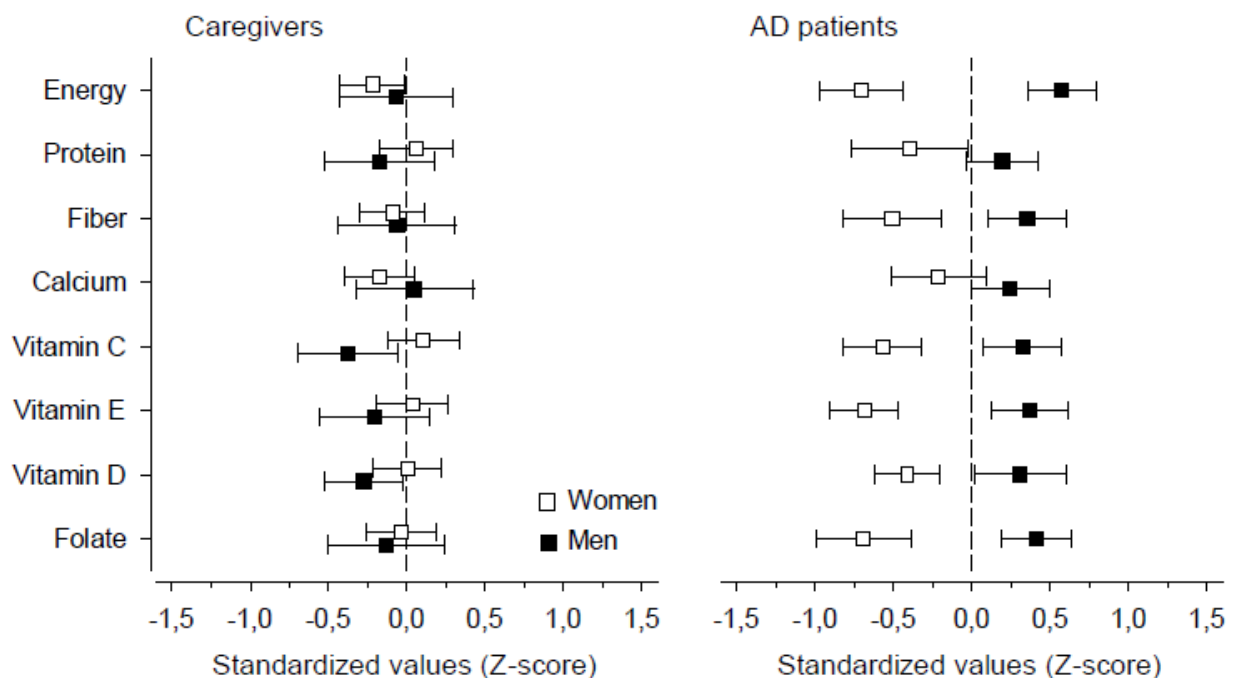


Figure 6. Standardized values of energy and nutrient intake among the caregivers and those with AD

Figure 6 presents the standardized values of energy and nutrient intake among the caregivers and those with AD, and clearly shows the gender differences in nutrient intake, especially among the latter.

5.4 The effectiveness of the intervention (Article 3)

The effectiveness of the tailored nutritional guidance is discussed with reference to those with AD. In addition, 28 (70%) of them received ONSs tailored to their needs and supplied for between four and 12 weeks. Those with a low protein intake were offered ONSs with 20g of protein and 200 kcal, and those with weight loss were offered ONSs containing 10g protein and 300 kcal.

Weight change

The intervention had no effect on the participants' weight, and the changes in body weight between the IG and the CG did not differ statistically ($p = 0.68$). At baseline, the mean weight of the men in the IG was 78.1 (SD 10.9) kg, and 68.6 (SD 12.9) kg among the women. The respective weight increases were 0.9 kg (95% CI 0.2 to 1.6, $p = 0.013$) and 1.3 kg (95% CI -0.3 to 2.8).

Nutritional status

Baseline nutritional status measured in accordance with the mean MNA at baseline was 23.7 (2.1) in the IG and 24.2 (2.2) points in the CG. The mean MNA decreased during the intervention, the change being -1.3 (95% CI -12.3 to -0.2) in the IG, and -1.1 (95% CI -1.9 to -0.3) in the CG, neither of which was statistically significant ($p = 0.76$). However, the MNA improved in 34 percent of those with AD and 25 percent of those in the CG.

Nutrient intake

The intervention improved the nutrient intake of those with AD, and the difference in the mean change of nutrient intake between the IG and the CG was statistically significant for protein ($p = 0.031$) and calcium ($p = 0.025$). The mean protein intake increased by 0.08 g/bodyweight (kg) in the IG and decreased by 0.06 g/bodyweight (kg) in the CG. The mean calcium intake increased by 85 mg in the IG, and decreased by 16.6 mg in the CG. The intervention also positively affected other nutrients (vitamin C, vitamin E and folate), but the difference between the groups was not statistically significant. Figure 7 shows the changes in nutrient intake between the IG and the CG in terms of effect size.

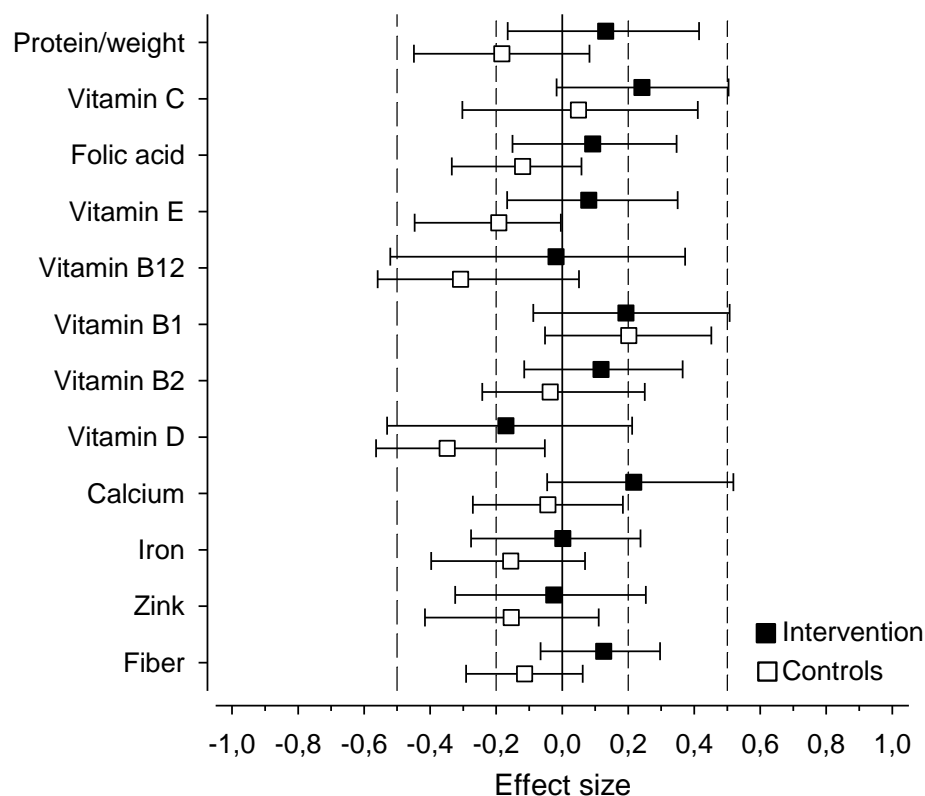


Figure 7. Changes in nutrient intake in the intervention and control groups by effect size

Health-related quality of life

The intervention had positive effects on the HRQoL of those with AD, measured on the 15D instrument. The total 15D score showed a statistically significant ($p = 0.007$) difference between the IG and the CG: it increased in the IG by 0.006 (95% CI -0.016 to 0.028) and decreased in the CG by 0.036 (95% CI -0.016 to 0.028), and the difference in changes between the IG and the CG was significant ($p = 0.007$). The 15D dimensions showing inter-group differences included *breathing* 0.036 [95% CI -0.014 to 0.086] in the IG and -0.035 [95% CI -0.087 to 0.016] in the CG ($p = 0.048$), *usual activities* -0.009 [95% CI -0.074 to 0.056] in the IG and -0.086 [95% CI -0.153 to -0.019] in the CG ($p = 0.046$), *mental functioning* 0.012 [95% CI -0.044 to 0.069] in the IG and -0.11 [95% CI -0.17 to -0.049] in the CG ($p = 0.006$), and *depression* 0.037 [95% CI -0.010 to 0.084] in the IG and -0.030 [95% CI -0.079 to 0.020] in the CG ($p = 0.045$). The analyses were adjusted for age, gender, baseline BMI and MMSE. Usual activities reflect ADL performance, whereas mental functioning is related to cognition.

Falls

The number of falls measured in accordance with the fall diaries differed between the IG and the CG over the one-year intervention: those with AD in the IG had 31 falls whereas those in

the CG had 63: the respective mean numbers of falls per person were 0.55 [95% CI 0.34 to 0.83] and 1.39 [95% CI 1.04 to 1.82], $p < 0.001$.

5.5 The feasibility of the intervention (Article 4)

The aim in the qualitative analysis was to describe the positive elements that enhanced nutrition on the one hand, and on the other to point out the challenges encountered during the intervention and the factors that could prevent nutritional improvement. The qualitative analysis included the 40 couples in the IG who experienced the intervention. It was based on their feedback and the nutritionist's field notes on the home visits.

Feedback from the couples, mainly from the spouses, attested to the feasibility of tailored nutritional intervention. The majority of the participants (93%) evaluated the nutritionist's guidance as useful for them. The most highly valued form of guidance was discussion with the nutritionist (42%), but written materials such as the booklet on good protein sources and good nutrition for older adults were also rated as useful.

The positive elements that helped the participant to improve their nutrition and quality of life included a positive approach, home visits, group meetings and the use of ONSs. The challenges included having false ideas about nutrition, health problems, declining physical functioning, and inveterate eating habits (Table 14).

The couples experienced the home visits as feasible in terms of implementing nutritional guidance: some of the participants had functional disabilities and leaving home would have been too much of an effort for them. The visits were also uplifting for some of them, and left them with the feeling that someone cared. The group meetings had a socializing effect, and they also helped to reinforce the nutritional message. The provision of protein-rich snacks was a classic example of benefiting from constructive learning theory: the participants first encountered the snacks at the pleasant meeting, became interested in them and later on accepted them as a part of their daily diet. The use of ONSs was tailored to the participants' individual needs, and those who received them valued them. Several of them believed they had given them more energy and were better able to cope with their daily exercise routines. The renewed energy even motivated some to make changes in their diets.

The most important aspect of the intervention was how it was implemented. Some of the recipients were surprised at the positive approach. Many of them had very negative recollections of previous nutritional guidance. In this case the focus was on avoiding certain foods and losing weight. The positive approach and feedback encouraged the participants to share their opinions and ideas about nutrition more freely, which in turn created a positive learning environment and later on led to dietary changes. Practical suggestions were given, but they were based on their own wishes and ideas.

Some of participants had false ideas and inveterate eating habits that hindered nutritional improvement. Others were concerned about weight gain, and believed they should lose

weight, or that they should avoid all fat. Some had even received conflicting nutritional guidance on weight loss from healthcare professionals. Problems such as celiac disease and swallowing difficulties also hindered nutritional improvement. Some men found cooking an overwhelming task, and functional disabilities prevented some from doing grocery shopping. Table 14 summarizes the results of the qualitative analysis (Article 4).

Table 14. Positive elements promoting improved nutrition, and challenges hindering nutritional improvement

POSITIVE ELEMENTS PROMOTING IMPROVED NUTRITION AND QUALITY OF LIFE			
Positive attitudes to nutrition	Home visits	Group meetings	Oral nutritional supplements (ONSs)
<ul style="list-style-type: none"> - findings from food diaries interesting - positive feedback - practical suggestions - participant-centered approach 	<ul style="list-style-type: none"> - convenient - feeling that someone cared 	<ul style="list-style-type: none"> - socializing - reinforced the nutritional message - introduction to protein-rich snacks - sparked an interest in nutrition issues - taxi transportation enabled everyone to participate 	<ul style="list-style-type: none"> - regained energy - motivation to make dietary changes - motivation to exercise
CHALLENGES DURING THE INTERVENTION PROCESS THAT HINDERED NUTRITIONAL IMPROVEMENT			
False ideas about good nutrition	Health problems	Impaired physical functioning	Inveterate eating habits
<ul style="list-style-type: none"> - idealization of weight control - concerns about weight gain - conflicting guidance received previously - preconceptions of home-delivered meals - food was too expensive 	<ul style="list-style-type: none"> - celiac disease, swallowing and chewing problems - poor appetite 	<ul style="list-style-type: none"> - cooking an overwhelming task - inability to go out 	<ul style="list-style-type: none"> - refusal to eat any fruit or vegetables - obsession with avoiding fat

6. DISCUSSION

6.1 General observations

The studies reported in this dissertation were based on multiple methodologies. The investigation focused on nutritional status, and energy and nutrient intake as indicative of the nutritional problems of community-dwelling individuals with AD and their spouses in cross-sectional analyses. The association between the caregiver's gender and the AD subject's nutrient intake was also studied. The baseline findings facilitated the implementation of the tailored nutritional intervention. A RCT assessed the effectiveness of the tailored nutritional guidance on the weight, nutritional status, nutrient intake, quality of life and falls of the AD subjects, with a one-year follow-up to evaluate the true effectiveness of the intervention. Qualitative analysis enhanced current understanding of tailored nutritional guidance and its feasibility among AD families.

A total of 99 couples were included in the study. A low BMI was rare among the AD subjects: in only three percent of them was it under 20 kg/m²: among the rest, 23 percent had a BMI of 20-24 kg/m², 53 percent between 24-29 kg/m², and the remaining 21 percent over 30 kg/m². None of study participants were malnourished according to the MNA, although 44 percent of the AD subjects and 16 percent of the spousal caregivers were at risk of malnourishment, and 56 and 84 percent, respectively, had a good nutritional status. The mean energy intake was at a fairly good level, apart from among the females with AD. With regard to nutrient intake among all participants, however, the results were not very positive. First, it varied widely, and even if the mean intake was adequate, a large number of participants received less than the recommended amounts of several nutrients. Protein intake was below the 1g per bodyweight in about 71 percent of the women, and 47 percent of the men with AD. The respective figures for spouses were 49 and 71 percent. The intake of several vitamins, including vitamins C and E, and folate, were below the recommended levels. There were lower levels of nutrient intake in families with a male caregiver, especially among the female AD subjects. However, no differences in calcium intake were identified.

Tailored nutritional guidance improved the nutrient intake and the quality of life of those with AD. In addition, the IG reported a lower falling rate than the CG during the one-year follow-up. However, there was no intervention effect on the primary outcome: weight change. Positive feedback from the participants attested to the feasibility of this tailored nutritional guidance. The positive elements of the intervention included the positive attitudes towards nutrition, the home visits, the group meetings, and the use of ONSs. Challenges that hindered dietary changes included health problems, false ideas about nutrition, impaired physical functioning and inveterate eating habits.

6.2 Methodology

Strengths

Several strengths of present study are worth mentioning. First, it was based on a randomized, controlled design. The randomization succeeded well, and the groups were similar at baseline. In addition, the study population was gathered from the drug reimbursement register, which confirmed the AD diagnosis of the participants. Another strength is that we were able to conduct a comprehensive investigation of nutrition in community-dwelling AD families, and to obtain information on nutrient intake from this challenging group of older adults. Complementing the quantitative data on nutrient intake and the effectiveness of the intervention was the qualitative data we obtained on the feasibility of the intervention and the challenges. Qualitative data was obtained from the nutritionists' field notes and the participants' feedback questionnaires. This data facilitated deeper consideration of the intervention process and its feasibility, and of its implementation as part of daily care among this growing target group.

A further strength is the use of well-validated methods. Nutritional status was measured in accordance with the MNA, which has been validated for older adults (Vellas et al. 1999) and has been used in several populations (Guigoz 2006, Kaiser et al. 2010). The 15D questionnaire measuring HRQoL is a generic measure, but has been successfully used in studies on people with AD, with the help of caregivers (Strandberg et al. 2006b, Pitkala et al. 2008, Pitkala et al. 2013). Information on falls was retrieved from the caregivers' diaries, which was considered a more dependable method than retrospective measurement (Hannan et al. 2010). The MMSE (measuring cognition) was used as background information (Folstein et al. 1975). It was shown in validation studies that MMSE scores did not change among about 25 percent of demented individuals in a one-year follow-up, and that it was not sensitive to change in interventions (Tombaugh 2005). Its strength is that it is short and easy to administer, and is therefore widely used. The CDR measure of the dementia stage was also used as background information (Hughes et al 1982), and its repeatability has not been studied (Berg et al. 1993).

Detailed food diaries were collected from the participants, and this facilitated the calculation of nutrient intake. To our knowledge, this is the first RCT study to explore nutrient intake among AD families. Shatenstein (2008) collected food diaries from community-dwelling AD subjects with the help of their spouses, but the results of her intervention were only reported in two case studies. Collecting food records from individuals with AD is a challenging task because it requires cognition on their part (van Staveren et al. 1994). In this study the spousal caregivers were the key elements in ensuring the gathering of reliable food records from the couples, and they were very diligent in this task. Indeed, food diaries are considered suitable for older people (Gariballa & Forster 2008), and it is suggested in a validation study that older adults up to the age of 80 perform well in dietary studies (Rothenberg 2009). In addition to facilitating the measurement of nutrient intake, food diaries play a useful role in nutritional education (Gariballa & Forster 2008), which was the aim of this intervention. The use of the

Nutrica program to calculate nutrient intake was appropriate in this study because it covers a wide range of basic Finnish foods, and has been used in other studies (Suominen et al. 2004).

Limitations

This study has some limitations. The fact that the intervention targeted diagnosed AD patients means that the findings cannot be generalized to people with other types of dementia. Furthermore, of those receiving the recruitment letter from Kela, only a small proportion agreed to participate, indicating some selection bias. We would also have benefited from a bigger sample size given the number of intervention dropouts (21%) during the year. Moreover, food diaries may contain flaws, and therefore they were all checked by phone. It is suggested in some studies that food diaries may underestimate food intake by 10-15% (de Vries et al. 2009), and that the act of registering food intake may change usual food habits (van Staveren et al. 1994). Thus, members of the CG were also asked to keep food diaries, which may have diluted the differences between the groups. The diaries were kept over three days, which may not be long enough to show average food intake over a longer period. The food intake of the participants was widely discussed during the home visits, and it appeared that their food habits were very stable. Food diaries are typically collected for between one and seven days, and three days is estimated to be an average time (van Staveren et al. 1994). In this case we thought three days would be the maximum time without putting extra stress on the spouses. The food diaries used in this study were meticulously kept, they were checked by phone, and the participants' food habits were discussed during the home visits. It could be concluded from the above that the method worked well in this case.

6.3 The findings

At baseline, the majority of AD subjects were men, and they were slightly older with more comorbidities and medications than their spouses. The mean MMSE score was 19 and the majority were in the mild-to-moderate stage of AD according to the CDR. In other words, they were at an earlier stage of the disease than the informants in the studies conducted by Riviere et al. (2001), Lauque et al. (2004), Pivi et al. (2011), and Salva et al. (2011), in which the mean MMSE score varied between 12 and 15. Over 70 percent of all participants had a BMI of 20-29 kg/m², 24-29 kg/m² being considered suitable for older adults (Suominen et al. 2014). The overall mean number of years of education was about ten, indicating a fairly well educated population. This is in line with some previous studies, indicating that the more highly educated are more likely to participate in intervention studies (Wettstein et al. 2004). The participants were also interested in their own health and nutrition, which were their main reasons for participating in the study according to the feedback questionnaire. It may be that the nutrition of the average population of community-dwelling older adults is even worse than indicated in the present study.

Nutrition at baseline

Nearly half of our AD participants were at risk of malnutrition, although none of them were malnourished. This is in line with findings reported in many studies conducted among community-dwelling older adults with AD (Spaccavento et al. 2009, Saragat et al. 2012, Roque et al. 2013), although some have shown higher malnutrition rates among AD subjects (Rullier et al. 2013). The MNA is widely used to screen and measure malnutrition among older adults (Guigoz et al. 2002), and population studies show higher rates of malnutrition among those with AD than among healthy older adults (Kaiser et al. 2010). This study population was very heterogeneous in terms of nutrition: some couples had very healthy eating habits and good nutrient intake, whereas others struggled with food-related activities and this resulted in poor nutrient intake.

The mean energy intake of the women with AD was very low, only about 1,300 kcal per day. This is low even taking into account possible underreporting, and it is challenging to receive enough nutrients with that energy level (de Groot et al. 1999). A low protein intake was striking among these women, and does not maintain good nutritional and functional status (Morley et al. 2010, Bauer et al. 2013). Energy and nutrient intake among the caregivers in this study was lower than reported in studies among healthy older adults, although these study populations appear to be healthier than average (Volkert et al. 2004, Jungjohann et al. 2005). An earlier Finnish National Nutritional survey reported fairly low daily energy intake of 1,480 kcal among older women, but the mean nutrient intake was below the recommended levels only for vitamin D, folate and iron (Helldan et al. 2013).

A large percentage of those with AD and their spouses had a low intake of several nutrients, which in the case of protein, vitamins C and E, and folate indicates a poor diet quality. This is worrying because these essential nutrients are known to be important for immunity, and for maintaining muscle mass and functional ability (Bauer et al. 2013). The heterogeneity of nutrient intake is also evident in large epidemiological studies among healthy older adults, in which, as in ours, the mean intake is adequate, but a large proportion of the participants have less than enough of some nutrients (Marshall et al. 2001, Volkert et al. 2004, Jungjohann et al. 2005, Toffanello et al. 2011). Inadequate nutrient intake has also been reported among community-dwelling individuals with early-stage AD (Shatenstein et al. 2007), and reflects the results of studies reporting low plasma levels of several nutrients among AD subjects even when energy and protein malnutrition was not present (Lopes da Silva et al. 2014). This could also be indicative of the elevated need for or changed bioavailability of certain nutrients among people with AD (Mi et al. 2013, Lopes da Silva et al. 2014).

The male gender of the caregiver was strongly associated with poor nutrient intake in the AD families. The male caregivers involved in this study were older, had more comorbidity and tended to have more disabilities than the female caregivers. These factors may also affect their own food intake. However, they reported a lighter burden than the female caregivers. This is in line with an earlier Finnish study investigating gender differences in caregiving in

which the authors suggest that men experience their caregiver role differently to women (Poysti et al. 2012). Gender differences may also be present in the filling in of food diaries in that women may be more precise. All the food diaries analyzed in this study were carefully checked and discussed, and the men managed them well. The increased level of stress (Glaser et al. 2001, Gouin et al. 2008) and comorbidity (Kiecolt-Glaser et al. 1991, Shaw et al. 1999, Dauphinot et al. 2015) among caregivers reported in several studies may have an effect on their nutrition. The mean Zarit score among the caregivers in this study indicated a light or average burden. The variation was large, however, thus the association between the caregiver's stress and nutrition should be further investigated.

Poor intake of several nutrients, such as vitamins C and E, and folate, was widely observed in families with a male caregiver, especially among women with AD. This indicates a low intake of fruit, vegetables and wholegrain products, and the finding is in line with the findings reported by Presse et al. (2008) of the low consumption of fruit and vegetables among people with AD. The proportion of both AD subjects and spouses with a low vitamin-C intake was contradictory to the findings of previous studies among healthy older adults (Volkert et al. 2004, Helldan et al. 2013), although Presse et al. (2008) reported lower fruit and vegetable intake among AD subjects compared to cognitively healthy controls (Presse et al. 2008). Some couples in this study had a very monotonous diet and tended to eat the same food items day after day, thereby putting themselves at a high risk of insufficient nutrient intake.

It has been reported in previous studies that older men to have a poorer diet quality, and especially a lower intake of fruit and vegetables than females (Bates et al. 1999, Baker & Wardle 2003). Poor cooking skills are among the assumed reasons behind the low vegetable intake (Hughes et al. 2004). Indeed, it was observed in the present study that the low protein intake among the females with AD tended to reflect the replacing of meals with bread and snacks. A poor income was also associated with poor protein intake at baseline. Furthermore, home visits revealed that many male caregivers were not familiar with household activities. Nevertheless, they were generally very keen to take part in the intervention, and were willing to learn more. This is in line with the results of a study conducted by Keller et al. (2008) indicating that male caregivers are very concerned about the nutrition of their AD spouses.

The effectiveness of the intervention

Weight change was set as a primary outcome measure, as in earlier studies with similar populations as this one (Riviere et al. 2001). No differences in weight change between the groups could be attributed to the intervention. Weight change may not have been a suitable measure in the present study in that only a few of the participants had a low BMI and there was therefore a relative ceiling effect among them. Other outcomes should be considered in future studies, as weight loss may be more prevalent in more advanced stages of AD (Droogsma et al. 2015). The intervention had no significant effect on *the MNA*. One reason for this could be that none of the participants were malnourished to start with, and 44 percent of those with AD were at risk of malnutrition. There was an improvement in MNA for some, however, which indicates successful tailored guidance.

The *nutrient intake* of the AD subjects improved after the intervention. To our knowledge, this is the first study to explore the effect of nutritional guidance on nutrient intake. The improvements were widely visible, but the differences between the groups were significant only with regard to protein and calcium. This may have resulted from the increased consumption of milk products in the form of snacks, which is in line with the results reported in Iuliano et al. (2013) indicating that adding two additional servings of milk products is a feasible way of improving nutrient intake among elderly residents. We used brochures containing pictures of good protein sources in our intervention, and this helped the education process. Brochures tailored to older adults have also proved feasible in earlier studies (Shatenstein et al. 2008). Some participants received ONSs for a short period of time, but they were no longer being distributed when the food diaries were collected at the end of the study and thus their use does not explain the increased protein intake.

This is the first study to investigate the effects of nutrition intervention on *HRQoL*. There was a significant difference in HRQoL between the IG and the CG measured in accordance with the 15D questionnaire (Sintonen 2001): the difference of 0.04 points in the total 15D score could be described as significant, given that a change of 0.02 to 0.03 is considered to be clinically relevant (Sintonen 2001). Improvements in dimensions such as usual activities, depression, breathing, and mental functioning were also detected. The improvement in quality of life could be attributable to various factors. The increased intake of protein seemed to brighten up some participants who found new energy and started to do a little exercise. This may have been reflected in their muscle function, which in turn could have affected their breathing, daily activities, mood and mental functioning. Improved nutrition may indeed affect mood and mental functioning, but these findings remain to be confirmed in future studies. However, factors other than improved nutrition may have affected the quality of life of our study participants. It is also possible that the home visits from the nutritionist cheered them up and put them in a better mood.

Those with AD in the IG had fewer *falls* than those in the CG during the one-year follow-up. The falls were self-reported in the fall diary kept by the spousal caregiver, and could therefore have contained flaws, but the randomized design should have ensured the equal treatment of the IG and CG in this respect. The reason for having fewer falls may have been connected with the better physical functioning of those in the IG. Tieland (2012) reported improved physical functioning among older adults using ONSs in the form of a 15g dose of protein twice a day. Physical exercise has been found to decrease the number of falls among AD subjects (Pitkala et al. 2013, Burton et al 2015), but these trials did not include tailored nutrition intervention. In another RCT, ONSs, calcium and vitamin D supplementation, supported by nutritionist counseling, succeeded in decreasing the number of falls among malnourished elderly adults following discharge from hospital (Neelemaat et al. 2012). Future studies should assess the effectiveness of nutrition and exercise combined in preventing falls, both of which are also known to help in preventing and treating frailty and sarcopenia among older people (Cruz-Jentoft et al. 2010, Bauer et al. 2013, Cesari et al. 2014).

There are few reports of tailored nutritional interventions among community-dwelling AD subjects. To my knowledge, only four nutritional trials with a randomized, controlled design have been conducted among community-dwelling individuals (Lauque et al. 2004, Planas et al. 2004, Pivi et al. 2011, Salva et al. 2011). Lauque et al. (2004) found that ONSs increased energy and protein intake, as well as weight and fat-free mass, and Pivi et al. (2004) reported a weight increase following the use of ONSs. The post-intervention increase in energy levels Planas et al. (2004) refer to was not surprising given the prescribed daily intake of ONSs containing a total of 500 kcal. In addition, ONSs containing micronutrient supplementation has been found to decrease serum cholesterol levels (Planas et al. 2004). The teaching and training intervention Salva et al. (2011) describe succeeded in improving the MNA of their participants. Riviere et al. (2001) also found that educating caregivers had a positive effect in terms of weight gain among their charges, but the study was not a RCT. No improvement in functionality has been reported (Lauque et al. 2004, Salva et al. 2011). Methodological questions arise in some of these studies. Those of Pivi et al. (2011) and Planas et al. (2004) lack information on the power calculations, and on the randomization process. Planas et al. (2004) discuss several outcomes, but the primary ones were not set, and the drop-outs were not reported. None of these studies investigated the effect of intervention on the quality of life or falls.

Some studies examined the effect of nutritional supplements on cognition among AD subjects, but no positive results have appeared (Freund-Levi et al. 2006, Sun et al. 2007, Aisen et al. 2008, Chiu et al. 2008), although there have been references to the negative effects of antioxidant supplementation on cognition (Lloret et al. 2009, Galasko et al. 2012). These studies were short in terms of timescale, with small numbers of participants, but even a recent study with a long follow-up (5 years) reported no effect of omega-3 fatty acid and antioxidant supplementation on cognitive functioning among cognitively intact participants with age-related macular degeneration (Chew et al. 2015). Medical foods including several nutrients have had some positive effects on verbal tasks and NTB memory among people with very mild AD (Scheltens et al. 2010, Scheltens et al. 2012), but the effects on those at a more severe stage of the disease remain to be seen. It is also worth noting that some community-dwelling AD sufferers and their spouses with poor dietary habits may have real nutritional deficits, in which case supplementation would be essential and beneficial. The dietary and food habits of this population vary considerably, therefore tailored, comprehensive nutritional assessment and guidance should be available to all AD families.

The feasibility of the intervention

The positive feedback from the participants attested to the feasibility of the intervention. According to the findings of the qualitative study, the elements that enhanced the participants' nutrition included constructive feedback, home visits, group meetings, and ONSs. ONSs have been successfully used in treating weight loss, mainly among institutionalized individuals (Hanson et al. 2011), and have positively affected the nutritional status of AD patients recovering from acute illnesses in a hospital setting (de Sousa & Amaral 2012). The challenges

in this intervention included the health problems and diseases that adversely affected daily life and nutrition in the families. Some participants had inveterate ideas and food habits, which hampered our nutritional guidance and suggestions. However, guidance was always given in a positive manner. It involved discussing matters with the participants and taking into account their own opinions, in line with the reflective learning model (Spencer et al. 1999, Dolmans et al. 2005).

Home visits were essential in terms of implementing the tailored nutritional guidance, and were convenient for our participants who already had some functional limitations. They have not featured in interventions among those with AD, however. Home visits also entail social activation for the couples, and the group meetings aimed to reinforce the nutritional message and to give peer support. Nutrition interventions involving active participation have yielded promising results among community-dwelling older adults (Bandayrel & Wong 2011). The participants also valued the meetings according to the feedback they gave. It was also encouraging that after the group meeting in which healthy and protein-rich snacks were provided, many participants found similar items in grocery stores and included them in their daily diets. The value of using practical suggestions and incentives has been discussed in previous studies (Sahyoun et al. 2004, Shatenstein et al. 2008).

The favorable results reported in this study may be attributable to the fact that our nutritional guidance was tailored to the participants' needs. In terms of feasibility it seems that personal nutritional guidance is a good approach among community-dwelling AD couples. Changes in diet are possible, but it may require several attempts. ONSs may be used as part of the tailoring, and not just to complete the nutrition but also to motivate the participants to exercise. The feedback received from the post-intervention questionnaire was positive, and the majority of participants felt that they benefited from it. This is in line with findings from previous studies on interventions among older adults indicating that they show an interest in nutritional issues and their health (Bandayrel & Wong 2011, Pogge et al. 2013). Furthermore, interventions should be tailored to participants' needs and interests (Higgins & Barkley 2003), and psychosocial aspects should also be considered (Moniz-Cook et al. 2011). A Finnish study reported, however, that services do not always meet the needs of people with AD and their families (Raivio et al. 2007). Many of the male caregivers in this study population would have benefited from practical cooking classes (Keller et al. 2004a), and many female caregivers would probably benefited from psychosocial and peer support. A review investigating non-pharmacological interventions among AD families concludes that multicomponent interventions may be a useful and also a cost-effective way of improving their quality of life (Olazaran et al. 2010).

Given the growing population of older adults, it is necessary to find ways of preventing cognitive and functional decline. Studies investigating the effect of nutritional intervention on cognition indicate that adopting a healthy lifestyle, including adequate nutrition, may delay the onset of dementia (Ngandu et al. 2015). Both those with AD and their spousal caregivers are prime targets for intervention in community-dwelling AD families. AD prevention is still

feasible among spouses, and their charges could benefit from improved functionality and quality of life. It could therefore be concluded from the findings of this study that older adults should be screened for nutrition at an early stage, and that the screening should focus not only on weight but also more precisely on dietary quality. Nowadays, the early diagnosis and treatment of AD may be one reason why weight loss is not widely present in the early stage of the disease (Droogsma et al. 2015). The present study shows that a poor diet and inadequate nutrient intake may still be present, and without intervention may lead to malnutrition. The results also show that it is possible to improve the nutrition and, more importantly, the quality of life of people with AD. Community services targeting AD families should include nutritional advice, exercise and social activities, and families could choose the activities that best suit their needs.

7. CONCLUSIONS

Community-dwelling older adults with AD and their spousal caregivers are a heterogeneous group in terms of nutrition, and their nutrient intake may well not comply with the recommendations. Inadequate protein intake was common in that the majority of participants did not achieve a daily intake of 1 gram per kilogram of body weight. The intake of several essential nutrients such as vitamins C and E, and folate was also inadequate among many of them.

The baseline results revealed a gender difference in nutrition among AD families, especially among females with AD. Nutrient intake was significantly poorer in families with a male as opposed to a female caregiver. Tailored nutritional intervention had no effect on the weight of the AD subjects, but it improved their nutrient intake and HRQoL and reduced the number of falls.

The intervention was feasible in that the majority of couples accepted it, and believed they had benefited from it. The positive approach of those offering tailored nutritional guidance empowered the couples, and furthermore led to positive dietary changes.

The nutrition of community-dwelling individuals with AD should be assessed regularly, and tailored nutritional guidance should be offered to those who need it. In many cases, small additions to the diet could improve its quality. ONSs could be used in addition to nutritional guidance.

8. IMPLICATIONS FOR FUTURE STUDIES

This randomized, controlled trial showed improved nutrition and quality of life among individuals with AD, but further similar trials are needed to confirm the findings. Future research should focus on the effectiveness of nutritional guidance on patient-focused outcomes such as HRQoL and should investigate functionality. Nutrition should be investigated in more detail, assessing plasma nutrient intakes in addition to food records, for example. Cost-effectiveness, the use of health services, institutionalization and mortality are further outcomes to be considered.

Tailored nutritional guidance turned out to be well accepted and feasible. The intervention should be further developed to comply with the participants' own concerns related to nutrition, and should also include exercise and social aspects. The person-centered approach aimed at empowering and supporting self-management skills should also be further explored. Caregivers may also be at risk of malnutrition, and may have inadequate nutrient intake.

There is thus a need for further randomized controlled trials focusing on their nutrition. Men as caregivers in this age cohort may need special support in food-related activities. They could benefit from cooking classes with nutritional information targeted specially at them, for example. Again, a randomized, controlled design would be appropriate for this kind of intervention.

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